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NAME OF AUTHOR/*NOM DE L'AUTEUR* Thomas Heckmann

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NAME OF SUPERVISOR/*NOM DU DIRECTEUR DE THÈSE* Dr. Charles Bourassa

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DATED/*DATÉ* 20 January 1978 SIGNED/*SIGNÉ* Thomas Heckmann

PERMANENT ADDRESS/*RÉSIDENCE FIXE* Department of Physiology
University of Alberta
Edmonton Alberta

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MOTOR EFFECTS OF SELECTIVE LESIONS IN THE DORSAL COLUMN NUCLEI OF THE CAT

by

© THOMAS HECKMANN

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH

IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE

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The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, for acceptance, a thesis entitled, "Motor Effects of Selective Lesions in the Dorsal Column Nuclei of the Cat" submitted by Thomas Heckmann in partial fulfilment of the requirements for the degree of Master of Science in Psychology.

Supervisor

External Examiner

Date 7 January 1978

ABSTRACT

Much evidence suggests that the Dorsal Column Nuclei may be divided anatomically into two subdividisions possessing different functional properties. One of these subdivisions allegedly relays somatosensory information to cortex. The other allegedly integrates such information into movement. The present work demonstrates that lesioning the alleged motor-integrative zone produces motor deficits. Lesions to the alleged sensory-relay zone produce less severe deficits. It can be argued that the relay-zone lesion deficits are due to incidental lesion involvement of afferent inputs into the motor-integrative zone. Lesions of the Medial Lemniscus, the output pathway from the sensory-relay zone, produce comparatively mild motor deficits. Thus sensory-relay zone outputs may not be as significantly involved in motor integration as are motor-integrative zone outputs.

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CHAPTER 1

INTRODUCTION

Recent research and theory questions the "classical" opinion that the dorsal column-medial lemniscus system of the spinal cord and brainstem is the sole ascending pathway which participates in finely resolved somesthetic discrimination (Wall, 1970, 1975; Wall & Dubner, 1972). Lesions of the dorsal columns (DC) in several species have, except under certain special conditions, failed to produce any lasting sensory deficit, yet such lesions have repeatedly caused enduring motor debilitation. Such results have led some workers to propose that the DC have no sensory function at all. Instead, the DC are seen as providing one of many exteroceptive pathways for feedforward of information used in the selection, activation, and control of centrally organized motor programs (Dubrovsky & Garcia-Rill, 1973; Dubrovsky, et al., 1971; Melzack & Bridges, 1971; Melzack & Southmayd, 1974; Wall, 1970, 1975).

Both the classical and "motor control" views receive much inferential support from physiological and anatomical evidence. A careful review of the negative behavioral evidence regarding sensory function of the DC shows that the evidence neither substantially confirms nor denies the classical concept of that function (Beck, 1975, 1976a). A few very recent experiments moreover have demonstrated lasting sensory deficits following DC lesions, but only when sensory tasks involve the discrimination of subtle tactual differences which are produced by movement of discriminanda over the sensory surface (Azulay & Schwartz, 1975; Vierck, 1974).

The two kinds of behavioral deficits produced by DC lesions, along with supporting physiological and anatomical evidence, suggest the dorsal column-medial lemniscus system provides afferent inputs which are utilized in at least two interrelated functions: (1) The analysis of spatial and temporal motion-generated stimulus transformations as complex "adequate stimulation" for refined discriminatory behavior. (2) The initiation and control of complex integrated movement.

The following chapters will: (1) Review the physiological, anatomical, and behavioral evidence for and against the classical position. Evidence in support of the motor control position will likewise be considered. It will be shown that the two positions are complementary rather than incompatible. (2) Review evidence suggesting that the two functions proposed for the DC system depend on interrelated yet distinct anatomical substrates which are dissociable at the level of the dorsal column nuclei (DCN). (3) Present procedures designed to take advantage of this dissociability in order to determine whether lesions to the substrate implicated in motor function bring about deficits in that function, and if such deficits are different from any which may be produced by lesion to the alleged sensory substrate. (4) Report the results of implementing such procedures. (5) Discuss and criticize the procedures and results and suggest strategies for further research.

CHAPTER 2

FUNCTION OF THE DORSAL COLUMN SYSTEM

This chapter presents: (1) A description of the classical DC pathway and its presumed function. (2) The behavioral evidence which fails to confirm this function. (3) An analysis which shows that no conclusions may be drawn from the negative behavioral evidence. (4) Physiological and behavioral evidence for the involvement of DC afferents in the control of complex motor activity.

2.1 The "Classical" Dorsal Column System

A distinct group of longitudinally running fibres is visible in the dorsal spinal cord of vertebrates. The lateral edge of this dorsal column of fibres is marked by a sulcus which separates it from the lateral and anteriolateral quadrants of the cord. Dorsal roots penetrate the lateral edge of the DC. In reptiles, birds, and mammals, some of the DC fibres penetrate into the medulla. In the cat, chimpanzee, monkey, bush baby, sheep, raccoon, and man the DC and their brainstem projections are distinguished as two tracts on each side of the midline of the dorsal spinal cord. The fasciculus cuneatus runs laterally up the length of the dorsal cord and terminates in the nucleus cuneatus. The fasciculus gracilis runs medially, projecting to the nucleus gracilis. The two dorsal column nuclei begin in the dorsocaudal part of the medulla where their cell bodies begin to be differentiated from the fibres of their respective tracts. The nucleus gracilis extends rostrally to the level of the caudal pole of the vestibular nucleus, the nucleus cuneatus to the level of the caudal pole of the spinal vestibular nucleus. Fibres of the DC synapse in

the DCN. The post-synaptic fibres then course rostro-ventrally through the brainstem as the internal arcuate bundle, crossing in the decussation of the medial lemniscus (ML). These fibres continue forward and synapse in the somatosensory relay nucleus, the nucleus ventralis posteriolateralis (VPL). Fibres from the VPL then project to the primary somatosensory projection areas of the neocortex (Berman, 1968; Jenkins, 1972; Kappers, et al., 1960; Norton, 1969; Mountcastle, 1974; Verhaart, 1970). The term "dorsal column system" will be hereinafter used to refer to this projection pathway as a whole, from receptor to cortex.

Several major papers have reviewed an extensive physiological and anatomical literature which indicates that the dorsal column system possesses all the properties of a classical lemniscal sensory pathway (Albe-Fessard, 1967; Brown, 1973; Darian-Smith, 1969; Kruger, 1973; Mountcastle, 1961, 1974; Norton, 1969; Poggio & Mountcastle, 1960; Rose & Mountcastle, 1959). Specialized end-organs gather specific stimulus information from periosteum, joint capsules, muscle spindles, and hairy and glabrous skin receptors. A high degree of somatotopic organization, in which forelimb and hindlimb representation are emphasized, exists throughout the system's rostro-caudal extent. Recent studies have demonstrated a topical submodality representation as well, beginning before the level of the cervical cord (Dreyer, 1974). The density of representation within the system's projections is related to peripheral innervation density. The most densely innervated areas, which are the distal limbs and face, are represented by the DCN units with small peripheral receptive fields, most of which show

surround inhibition.

Conduction in the dorsal column system is rapid. The DC carry the largest myelinated sensory fibres. Recent research has determined that although the dorsal horns contribute many secondary inputs to the DCN by way of tracts in the dorsolateral cord and the spinal grey, the DC carry a higher percentage of first-order afferents to their medullary relay nuclei than do other ascending paths (Angaut-Petit, 1975; Dart & Gordon, 1973; Nijensohn & Kerr, 1975; Rustioni, 1973, 1974, 1976; Rustioni & Molenaar, 1975; Uddenberg, 1968b). Relay units in the DCN show short latencies to peripheral stimulation. They adapt rapidly, responding with short repetitive trains to brief stimulation. They recover quickly after prolonged stimulation. They follow repetitive stimulation at very high rates, compared to relay units in other pathways.

The entire dorsal column system, from periphery to cortex, resists barbituate, alcohol, and chloralose anesthesia.

Thus, according to the reviews, the dorsal column system rapidly and directly transmits from periphery to cortex in a synaptically secure "labelled-line" fashion in which information is highly resolved in terms of time, location, and submodality. Taken along with clinical neurological evidence that DC interruption in humans produces cutaneous, vibratory, and kinesthetic sensory deficits (Boshes & Padberg, 1953; Davidson & Wechsler, 1936; Netsky, 1953; Weinstein & Bender, 1940), these qualities have suggested to Mountcastle and Darian-Smith (1968) that, "What remains in the mechanoreceptive sphere after large-fibre dorsal column lesion is the capacity to recognize that mechanical

stimulation has occurred; it is no longer possible to specify exactly its location, intensity, or shape." Mountcastle (1974) lays special stress on the dynamic capacities of the dorsal column system for relaying information concerned with change and transformation over sensory surfaces.

2.2 The Negative Sensory-Behavioral Evidence

A history of attempts to produce sensory deficits in experimental animals by lesioning the DC, reaching well back into the Nineteenth Century, has been reviewed elsewhere (Ferraro & Barrera, 1934; Sherrington, 1900; Wall, 1970). These early studies tended to use crude testing and histological techniques and were performed on a large number of different species. The results were diverse and contradictory and have little value at this time.

Recent research has failed to demonstrate any enduring detectable sensory deficit following DC or ML lesion in several species. DC and ML lesions in macaques, chimpanzees, and mangabeys yield only transient declines in weight discrimination performance (DeVito & Ruch, 1956; DeVito, et al., 1964; Sjoqvist & Weinstein, 1942). Transsection of the DC in macaques also fails to produce lasting performance deficits in two-point threshold, resolution of passively appreciated limb displacement, proprioceptive placing, vibrotactile detection, disc-size discrimination, and detection and localization of mild skin shocks (Christiansen, 1966; Eidelberg & Schwartz, 1971; Levitt & Schwartzman, 1966; Schwartz, et al., 1972; Schwartzman & Bogdonoff, 1968, 1969; Vierck, 1966, 1973).

Cats show at most only transient impairment in tactile placing,

localization, and detection following DC lesions (Diamond, et al., 1964; Lundberg & Norrsel, 1960; Tapper, 1970). They show a slight enduring deficit in roughness discrimination (Kitai & Weinberg, 1968).

Tactile detection in dogs is only transiently abrogated by DC section (Norrsel, 1966), as is performance in a postural control task (Reynolds, et al., 1971, 1972).

In humans, painful phantom limbs are usually only temporarily relieved by therapeutic DC lesion. A transient loss of vibrotactile sensitivity often accompanies the phantom limb relief (Browder & Gallagher, 1948; Pool, 1946). White and Sweet (1955) reported having "...never observed any significant neurological sequel from injury to the nucleus cuneatus."

After reviewing a portion of these negative results, Wall (1970) stated, "It is clear that deficits predicted by the classical theory are simply not seen." He furthermore concluded in the same and other papers that the DC serve no special role in sensation (Wall, 1970, 1975; Wall & Dubner, 1972). A consideration of issues of interpretation and methodology will show that such a conclusion is premature.

2.3 Interpretation of the Negative Evidence

2.3.1 Redundancy

Statements about the function or lack of function of lesioned pathways rest on inference rather than fact (Mountcastle, 1974). The inference in this case is that the dorsal column system plays no role in conscious sensation because deficits in sensation have not been detected following DC lesion. Other pathways, however, might carry physiologically or functionally redundant information to cortex.

The DCN are known to receive many inputs from the dorsal horns via the spinal grey and the dorsolateral tracts (sec. 2.1). Lemniscal properties are shared by fibres of the DC and many of the fibres in the dorsolaterally coursing spinocervical pathways. The fibres in these two pathways share inputs from the same receptor types, are both fast conducting, have a high synaptic security, contain units with small receptive fields and low absolute sensitivities, and share common thalamic projection sites (Christiansen & Levitt, 1964; Ha & Lui, 1966; Ha, 1971; Morin, 1955; Morin & Catalano, 1955; Morin, et al., 1963). The information conveyed in these paths may be redundant as, while neither DC nor dorsolateral lesions alone cause lasting sensory deficits in the studies already reviewed (sec. 2.2), combined interruption of them often does (Christiansen, 1966; DeVito & Ruch, 1956; DeVito, et al., 1964; Eidelberg & Schwartz, 1971; Kitai & Weinberg, 1968; Levitt & Schwartzman, 1966; Lundberg & Norrsell, 1960; Norrsell, 1966; Schwartzman & Bogdonoff, 1968; Tapper, 1970; Vierck, 1966, 1973).

Another factor in interpreting the results of DC lesions is that while hindlimb fibres carrying inputs from joints, muscle, and skin enter the DC at caudal levels, all but the fast adapting cutaneous fibres and a limited number of kinesthetic fibres pass out of the DC at the thoraco-lumbar border to synapse with cells of the horns (Whitsel, et al., 1970, 1972). Since equivalent forelimb inputs remain in the DC (Korn & Landgren, 1969; Oscarsson & Rosen, 1966), section of the DC at thoracic levels cannot be expected to have as serious an effect on hindlimb performance as cervical DC insult has on forelimb performance. In this regard it has been established that forelimb

motor deficits following cervical DC insult are more pronounced than hindlimb motor deficits following thoracic DC lesion (Denny-Brown & Gilman, 1963; Ferraro & Barrera, 1934; Gilman & Denny-Brown, 1966). Thus reports of no sensory deficit following thoracic level lesion cannot be used to support arguments that the DC do not carry certain information. Such information, while it initially enters the DC, may be shunted off to other functionally redundant, or even exclusive, pathways. Among the studies already reviewed, several used thoracic DC preparations (Lundberg & Norrsell, 1960; Norrsell, 1966; Schwartzman & Bogdonoff, 1968, 1969; Tapper, 1960; Vierck, 1966, 1973).

Wall (1970, 1975) has offered some compelling arguments against the concept of afferent system redundancy. These arguments, however, are based largely on certain teleological evolutionary assumptions best clarified and refuted by Noback and Shriver (1969).

2.3.2 Recovery

The capacity of the nervous system for functional recovery after insult is well known (Mountcastle, 1974). Geschwind (1974) has reviewed this capacity in regard to sensory systems subjected to massive subtotal lesions of afferent fibre tracts. Specifically in respect to DC function, Dobry and Casey (1972a) found that cats were easily able to learn and retain a roughness discrimination task after DC lesion if at least ten per cent of DC fibres remained intact.

Reasoning from such data, Beck (1975, 1976a) has argued that more than 90 per cent of DC fibres must be interrupted for DC lesion experiments to demonstrate a deficit. Most of the negative DC lesion studies either did not report lesion extent or showed less than 90 per cent

fibre interruption (Browder & Gallagher, 1948; Christiansen, 1966; Diamond, et al., 1964; Kitai & Weinberg, 1968; Levitt & Schwartzman, 1966; Norrsell, 1966; Pool, 1946; Tapper, 1970; Vierck, 1966; White & Sweet, 1955).

Thus recovery of sensory function after an initial transient deficit may be due to continuity of normal transmission through the few remaining inputs. Alternatively, it may depend on higher-level adjustment to the trauma. In this regard, Wall and Egger (1971) reported that a shift of thalamic unit receptive fields from hindlimb to forelimb representation took place in rats three days after thoracic fasciculus gracilis section.

As another alternative, recovery may be functional. That is, the same sensory information may be coded differently in physiologically dissimilar routes, which do not normally duplicate sensory function in intact animals. Or, different routes may carry information about different sets of cues. When one set of cues is attenuated by lesion, the animal is able to quickly re-form a sensory discrimination on the basis of the remaining sets of available cues. Unless special hypotheses are formed about the specific nature of such cues and tested with appropriate rigor, it will appear to the experimenter that the re-formed discrimination is the same, in terms of the phenomenology of the subject, as before the lesion. Such a "multiplicity of cues" is suggested by experiments with monkeys in which roughness discrimination was impaired by lesions to lemniscal cortical projection areas and tactile size discrimination was impaired by nonlemniscal cortical lesions. Lemniscal lesions did not produce size discrimination deficits and nonlemniscal

lesions did not cause roughness discrimination to falter (Semmes, et al., 1968).

A transient deficit, followed by recovery, may also be due to the wearing off of the immediate debilitating effects of surgical trauma such as edema, bleeding, and drug effects (Mountcastle, 1974).

The above considerations are intended to point out that a transient sensory deficit after DC lesion, followed by recovery, cannot be treated on a par with results of no deficit at all. It will be recalled (sec. 2.2) that transient deficits are characteristic of many of the "negative" sensory studies (Browder & Gallagher, 1948; Christiansen, 1966; Diamond, et al., DeVito & Ruch, 1956; DeVito, et al., 1964; Levitt & Schwartzman, 1966; Norrsell, 1966; Schwartz, et al., 1972; Vierck, 1973).

2.3.3 Adequacy of Stimulation and Testing

Beck (1975, 1976a) has drawn attention to the fact that lesion studies have not adequately sampled the alleged fine resolving properties of the classical dorsal column system by appropriate stimulating and testing techniques. Recalling the statement of Mountcastle and Darian-Smith (sec. 2.1), the classical theory does not predict the DC lesions will produce deficits in the simple appreciation of whether or not a stimulus has occurred. The theory predicts that discrimination based on the precise location, intensity, and shape of the stimulus will falter. The main critics of the classical position (Wall, 1970, 1975; Wall & Dubner, 1972), however, have condemned the theory on the basis of negative results in experiments using simple "on-off" detection or gross localization to widely separated body parts as the criteria for

"discrimination" (Browder & Gallagher, 1948; Diamond, et al., 1964; Eidelberg & Schwartz, 1971; Norrsell, 1966; Schwartz, et al., 1972; Schwartzman & Bogdonoff, 1968, 1969; Tapper, 1970). Two-point threshold was used in one negative study (Levitt & Schwartzman, 1966). Yet Vierck and Jones (1968) have shown that this test does not adequately sample the capacity of the skin for spatial resolution. Gross uncalibrated measures such as proprioceptive placing (Christiansen, 1966; Lundberg & Norrsell, 1960) may also be insensitive.

Two of the negative accounts utilized percutaneous electrical stimulation as the "adequate stimulus" (Eidelberg & Schwartz, 1971; Schwartz, et al., 1972). Yet Wall (1975) has argued that electrical stimulation sets up "unnatural" conditions of massive simultaneous volleying which may favor sensory detection in pathways not normally used. Similarly Beck (1975, 1976a) has stated that such stimulation provides ill-defined polymodal activation which is conveyed by pathways other than the DC. Thus studies utilizing electrical stimulation are of little value in assessing the allegedly refined lemniscal functioning of the dorsal column system.

2.3.4 The Critical Experiment--Isolated Dorsal Column

An appraisal of the recent findings of little or no sensory deficit following DC lesions makes it clear that these findings can be used neither to confirm nor to conclusively disconfirm a role of the dorsal column system in fine somesthetic discrimination. The findings are clouded by inadequate or absent histology, inadequate stimulation and testing procedures, and incomplete consideration of physiological data in their interpretation. Issues of redundancy and recovery have not

been appropriately dealt with.

A programmatic attack on issues of DC sensory function is required if definitive statements are to be made. The logical starting point for such a program would be an attempt to demonstrate the existence of sensory discrimination in preparations in which the DC have been isolated by anteriolateral cordotomy. If such could be demonstrated, it would then be possible to affirm that the classical position is valid, insofar as the DC do carry information by which sensory discrimination can be formed. Such preparations have so far been intentionally used in only three published studies and have provided apparently conflicting results.

Wall (1970) isolated the DC in rats at thoracic levels and found that the animals failed to behaviorally orient to pin pricks and pinches below the level of the anteriolateral lesion. Along with the review of negative sensory evidence in the same paper, this was used to support arguments against a sensory role of the DC. However, Meyers, et al., (1974) observed that thresholds of detection for whole-nerve electrical stimulation in cats were not altered by anteriolateral section. And in another study (Frommer, 1976; Frommer, et al., 1975), cats trained to detect light touch, discriminate the side of the body touched, discriminate the sizes of discs pressed onto the skin, and to discriminate the direction in which their fur was stroked, easily relearned these tasks with only the DC intact. Two cats were able to form the size discrimination with no training prior to DC isolation.

In a fourth study (Vierck, 1974) a small unilateral portion of the DC was left intact, and was the only ascending pathway remaining, after

an attempt to sever all ascending tracts at the thoracic level in the cord of one monkey. The animal demonstrated no loss in ability to detect a brush applied to the skin of the leg ipsilateral to the DC remnant. It also continued to discriminate whether the brush was stationary or moving, and the direction of its movement when moving. On the contralateral side, lesion to the DC alone was sufficient to permanently impair performance in the direction task, while the other two tasks suffered no deficit.

Taken together these reports suggest that the DC are both necessary and sufficient to provide the information required to form certain kinds of discriminations. While behavioral orienting was not seen in the rat study (Wall, 1970), neither was it seen in the cat discrimination study (Frommer, 1976; Frommer, et al., 1975) in which the animals nonetheless responded appropriately to stimulation by bar-pressing for rewards. Thus it appears that orienting, by itself, is not an adequate measure of whether a stimulus has sensory value. This is corroborated by evidence that, after initial training at levels of stimulation which elicit behavioral orienting, cats are able to respond at above chance levels to electrical stimulation of peripheral nerve trunks, sensory relay nuclei, motor nuclei and cerebellar nuclei at voltages well below those which will initially elicit an orienting response (Bourassa & Swett, 1967, and in preparation; Myers, et al., 1974; Swett & Bourassa, 1967).

Further implications of isolated DC experiments and their usefulness as part of a programmatic DC sensory function study will be taken up below (Chapter 6, Discussion).

2.4 The Dorsal Column System in Motor Control

Though few sensory deficits have been observed following DC lesions, certain types of motor deficits frequently occur. In addition, anatomical and physiological evidence suggest that the dorsal column system afferents are intimately involved in the feedforward and feedback regulation of complex motor acts. Some workers have thus rejected the sensory concept of DC function and substituted the notion that the system is involved in the initiation and smooth continuation of directed, complex motor activity. A role for the system in attentional processes relevant to its participation in the initiation of motor activity is also proposed.

2.4.1 Physiological and Anatomical Suggestions

Histological and electrophysiological studies in rats, cats, and monkeys have revealed many fibre projections from the DCN to targets implicated in the regulation and integrity of motor sequences. These targets include the dorsal and medial accessory olive nuclei, the zona incerta, the pontine protuberance of the brainstem, the red nucleus, the collicular plate, the cerebellar nuclei, the cerebellar cortex, and the quadrigeminate bodies (Anderson & Berry, 1959; Berkeley, 1975; Bowsher, 1958, 1961; Cooke, et al., 1971; Ebbeson, 1968; Gordon & Horrobin, 1967; Gordon & Seed, 1960, 1961; Gronewegen, et al., 1975; Hand & Lui, 1966; Hand & Van Winkle, 1975; Lund & Webster, 1967; Rinvik & Walberg, 1975).

Numerous studies have also outlined a variety of descending cortical influences mediated by the pyramidal pathway on evoked potential and unit activity in the DCN. These studies have been reviewed

elsewhere (Beck, 1975, 1976a; Kruger, 1973; Mountcastle, 1974; Norton, 1969; Towe, 1973; Wall, 1970; Wall & Dubner, 1972). The points essential to the motor control hypothesis are briefly summarized here.

Pyramidal fibres originating in the somatosensory cortex pre- and post-synaptically inhibit, post-synaptically facilitate, or sometimes have both inhibitory and facilitory effects on units of the DCN. Nuclear units of the kinesthetic submodalities such as joint rotation and muscle stretch are primarily facilitated. Units of the tactile submodalities such as hair displacement and light pressure are mostly inhibited. While conditioning stimulation to cortex causes inhibition and facilitation of evoked DCN unit activity, cortical influences apparently do not modify unit resting activity.

Evoked responses and evoked unit responses in the DCN of cats and rats are inhibited just prior to and during self-initiated movement (Ainsworth, et al., 1969; Coulter & Thies, 1971; Ghez & Lenzi, 1971; O'Keefe & Gaffan, 1971).

Recent work in cats has determined that corticocuneate projections have higher conduction velocities than corticegracile axons (Brech, et al., 1977). Also, corticofugal facilitation of cuneate units produced by post-cruciate electrical stimulation has less than one half the latency and duration of equivalent corticofugal influences on gracile units (Cole & Gordon, 1976).

The highly specific nature of cortical-pyramidal effects and the production of such effects by self-initiated movement might indicate that a special cortical "filter" operates over afferent input in the dorsal column system during movement. It may be that tactile

information is suppressed and kinesthetic information is facilitated. On the other hand, the inhibition of tactile units may be a way of increasing the resolution of afferent information during movement by increasing the sensitivity of units' inhibitory surrounds. Since the gracile pathway subserves hindlimb DC input and the cuneate pathway subserves forelimb input, this cortical filter may be temporally matched for the slower arrival of hindlimb impulses vs. forelimb impulses at the DCN, as the temporal differences in corticonuclear effects suggest.

Sotgiu and Cesa-Bianchi (1970, 1972) have found in cats that several of the nonspecific thalamic nuclei exert modulating influences on the DCN similar to but independent of the corticofugal effects. These effects are apparently mediated by the reticular formation rather than the pyramids (Sotgiu & Cesa-Bianchi, 1976; Sotgiu & Marini, 1977).

Although some workers have found evidence of DCN projections to the reticular formation (Anderson & Berry, 1959; Matzke, 1951; Hand & Lui, 1966), others have failed to confirm these observations (Bowsher, 1958; Lund & Webster, 1967). The existence of extralemniscal projections to thalamic nuclei other than the VPL is well established. Projections to the suprageniculate, medial geniculate, posterior, and intralaminar nuclear groups have been histologically and electrophysiologically indentified in several species (Anderson & Berry, 1959; Boivie, 1974; Bowsher, 1958; 1961; Curry & Gordon, 1972; Graybiel, 1972; Gordon & Jukes, 1964a, 1964b; Hand & Lui, 1966; Hand & Van Winkle, 1975; Keller & Hand, 1970; Lund & Webster, 1967; Rowe & Sessle, 1968; Whitlock & Perl, 1967).

Direct electrical stimulation of these nonspecific nuclei produces a behavioral orienting response which resists habituation, compared with the rapid habituation seen when the VPL is stimulated (Wester, 1971). Thus the dorsal column system inputs into these nuclei, though they are not the sole afferent inputs to them, may have attentional significance.

2.4.2 Behavioral Evidence

Though certain sensory deficits do follow DC lesion (see Chapter 3), they have only been observed under rigorous conditions of training, stimulation, task specialization, and testing. Motor deficits, which involve gross disruption of normal behavior, have been more commonly observed.

Insult to the DC at cervical levels in rats, cats, monkeys, chimpanzees, and humans leads to a number of clear and enduring disturbances of movement and the precise use of limbs. In general, reflexes become hypertonic, hypotonic, or are absent caudal to the lesion. The affected limbs are left in odd positions at rest, sometimes described as "catatonic". There is often a disturbance in locomotion, marked by shuffling, dorsoflexion of the feet, wide and wobbly stance, poor balance, splaying of the toes, broad footpad contact with the floor rather than stepping on the toes alone, and poorly timed stepping. Reaching and grasping is impaired and is sometimes characterized by "ballistic" movements of the limbs as if, once initiated, the reach goes through to completion without any fine feedback correction in progress. The severity of the deficit is related to the length and complexity of the behavioral sequence tested (Beck, 1973, 1976b; Boshes &

Padberg, 1953; Denny-Brown & Gilman, 1963; Ferraro & Barerra, 1934, 1935; Gilman & Denny-Brown, 1966; Dubrovsky & Garcia-Rill, 1973; Dubrovsky, et al., 1971; Melzack & Bridges, 1971; Melzack & Southmayd, 1974; Mettler & Liss, 1959; Myers, et al., 1974; Wall, 1970).

In respect to attentional function, Wall (1970) found that rats with DC lesions were deficient in one measure of behavioral orienting.

2.4.3 Resultant Proposals

The data summarized in the two previous sections have led to certain speculative proposals. The following is a summary and synthesis of these proposals, which were first put forward by Dubrovsky, et al. (1970), Melzack and Bridges (1971), Wall (1970), and Wall and Dubner (1972):

Because of its refined lemniscal properties, the dorsal column system provides the most rapid and precise route for inflow of information about posture, the location and position of the limbs in space and their relations to contactual surfaces, and ongoing changes in these brought about by movement. This information is provided to cortex in an unanalyzed and uncensored manner. Cortex then analyzes this input, using it to form an "hypothesis" about its sensory significance on the basis of information it provides about the relation of the current state of the body schema to previous experience and presently active immediate and distal goals of movement.

This is not an hypothesis in the sense of a rational mental act possessing intentionality. Rather it is an "hypothesis" in the sense used in certain information processing theories of perception (Miller, et al., 1961; Sommerhoff, 1974). In this sense it refers

to the establishment of an expectation of further input, the confirmation or disconfirmation of which will result in different sensory experience. Neurally, the hypothesis takes the form of selective filtering of slow-conducting nonlemniscal pathways, such that the channels for the "expected" inpingements are selectively enhanced. Wall (1970) has called this procedure of hypothesis formation and testing the "internal search."

If information arriving over the slower filter-controlled pathways matches the hypothesis, the relevant motor act follows. But if the information arriving over the DC has been insufficient to form an hypothesis, exploratory movements are initiated by cortex in order to generate new transformations in the dorsal column system, and hence more information by which an hypothesis may be formed. This process Wall (1970) has called the "initiation of external search."

Thus the dorsal column system is seen as a "central control trigger or feedforward limb of a larger feedback loop" (Melzack & Bridges, 1971) capable of exerting selective control of transmission over slower pathways. The information generated by the filtered inputs then feeds into a decision process which selects appropriate behavior from an array of pre-existing motor programs and which sequences these programs into a smoothly controlled act. The specific selection and execution of such programs also depends on visual, auditory, and other inputs which similarly exert filter-control over more slowly conducting systems.

Loss of the DC contribution to the selection of appropriate response sequences results in the activation of programs not precisely

adapted to the prevailing conditions of the ongoing situation. The organism is able to carry out sequential motor acts on the basis of information fed forward through the more slowly conducting systems, but there is a loss in the precision of the linkage of programs forming segments of the sequence. Hence observations that the severity of the motor deficit is related to the length and complexity of the motor activity tested.

2.5 Summary

Lesions of the DC have with few exceptions produced little or no enduring sensory deficit. On the other hand they have produced easily observed and lasting deficits in the performance of complex motor acts. The negative sensory data is questionable, since sensory function may fully recover after incomplete lesions or be mediated by other redundant pathways or processes; and since inadequate stimulation and testing has failed to address the sensory properties of the dorsal column system alleged by its physiological properties of fine spatio-temporal resolution. In addition, while one study has shown that the DC alone are not capable of mediating behavioral orienting, three other studies have demonstrated that both detection and discrimination are mediated by the DC, and in at least one case even in the absence of behavioral orienting.

Nonetheless certain workers have suggested that the DC do not participate in a sensory function. Citing physiological evidence for its involvement with motor activity as well as many experiments in which DC lesion produces motor deficits, they claim that its true function is to provide information to cortex which is used in the

selection and integration of motor programs in complex sequential acts.

Any assertion at the present time about a unitary function for the dorsal column system, be it in the sensory or motor realm, is premature. The following chapter reviews evidence that the sensory and motor functions of this afferent system are interrelated and interdependent, yet that they rely on distinct anatomical substrates the separate lesioning of which should affect the two functions differently.

CHAPTER 3

DUAL FUNCTION: INTERRELATEDNESS AND DISSOCIABILITY

This chapter presents evidence that the dorsal column system serves a special role in the conscious appreciation of fine differences in stimulation produced by movement. Physiological and anatomical evidence that motor and sensory functions depend on interrelated but distinct anatomical substrates is also presented. Experimental hypotheses are proposed, predicated on the possibility that these anatomical substrates are grossly dissociable by lesion. More specifically, it is proposed that lesion to one substrate will produce motor deficits of the type commonly observed with DC lesion and that lesion to the other substrate will produce no such deficit.

3.1 Dorsal Column Sensory Deficits

The few reports of enduring sensory deficit following DC lesion share the peculiarity that discrimination based on temporally sequenced--that is, moving--stimulation is involved.

Dobry and Casey (1972a) found that cats with near-total cervical DC lesions suffered a lasting inability to make alley choices based on the grades of sandpaper with which the alleys were paved. This finding is somewhat mitigated by apparent dorsolateral involvement in the animals most seriously affected.

Two sets of findings with monkeys are more clear. The finding of Vierck (1974), that DC lesion impairs the discrimination of movement direction differences while leaving simple detection of stimulation or differentiation of moving vs. nonmoving stimulation unimpaired, has already been covered (sec. 2.3.4). In addition, Azulay and Schwartz

(1975) found that when monkeys were trained to discriminate subtle tactile qualities of objects which were passively applied to the skin, this skill survived cervical DC insult. But if the same monkeys could learn a particular tactile discrimination only by actively palpating the discriminada, performance was permanently impaired. With certain discriminada, permanent deficits also occurred not only when discrimination required active palpation, but when passive learning of the discrimination required that the stimulus objects be moved over the hands and fingers of the monkeys by the experimenter.

These experiments suggest that the dorsal column system is specialized for, but not limited to, the mediation of subtle sensation differences generated by both actively generated and passively accepted motion. Physiological implications that the system is specially attuned for the transmission of rapidly changing spatiotemporal transformations will be recalled (sec. 2.1). Vierck's (1974) findings suggest an exclusivity for this function in the dorsal column system, since the thoracic level lesion which left DC fibres intact allowed only the limited number of fibre types carried to the DCN exclusively by the DC to remain (sec. 2.3.1).

In this light, the motor deficits observed after DC lesion (sec. 2.4.2) can be seen as complimentary, rather than opposed, to the notion that the dorsal column system subserves finely divided sensation: (1) Afferent inputs responsible for conveying information about spatiotemporal transformations of the body schema in respect of stimulus impingements are used in the planning and execution of motor sequences. These are the kinesthetic inputs. (2) Afferent inputs

responsible for providing information about stimulus impingements in respect of spatiotemporal transformations of the body schema subserve conscious discrimination. These are the cutaneous mechanoreceptive inputs. The conscious sensation is phenomenally experienced as relevant to the stimulus object property itself, rather than to the various stages of mechanoreceptive and kinesthetic integration which take place in the spinal cord, DCN, VPL, thalamic nonspecific nuclei, and cortex. Usually integration takes place in respect of self-initiated bodily movements. Passive appreciation of spatiotemporally transformed stimulation is simply the case when the body-transformation limb of this dual system of integration remains in a steady state.

These ideas are consistent with the fact that the most elaborate dorsal column systems are found in animals with highly refined digital manipulative capacities such as monkeys, raccoons, bush-babies, and human beings (Dreyer, et al., 1974; Johnson, et al., 1968; Pubols, et al., 1965; Welker, et al., 1964).

3.2 Motor-Sensory Dissociability in the Dorsal Column Nuclei

The previous section tentatively set forth the notion that the sets of afferents necessary for conscious sensation and for motor control may be respectively dichotemized into the mechanoreceptive and kinesthetic submodalities. The present section continues by reviewing anatomical and physiological evidence that fibres of these submodalities project to different areas of the DCN. These areas of the DCN are furthermore differentiated from one another in terms of cyto-architecture, the firing characteristics of their units, and their efferent and afferent relationships with other brain structures. These

further differentiations are also consistent with the idea that sensory and motor functions are served by distinct anatomical substrates. Much of the evidence has previously been reviewed by Beck (1975, 1976a), Kruger (1973), Mountcastle (1974), and Norton (1969).

3.2.1 Dual Cytoarchitecture

Ramon y Cajal (1909) reported that the DCN in higher vertebrates may be divided into two zones on the basis of cytoarchitecture. More recent histological studies in the cat, rat, and man have confirmed and enlarged upon these early observations.

In the cat, the first zone--here called the "relay zone" for reasons given below--hugs the dorsal surface of the medulla, penetrating no deeper than 1.2 - 1.6 mm. It begins rostrally about 0.5 mm. caudal to the obex (a triangularly-shaped membrane spanning the two sides of the caudal apex of the fourth ventricle) and continues caudally for about 4.0 - 7.0 mm. This zone contains large, rounded, 20.0 micron diameter cells with large, bushy dendrites. These cells cluster together into discrete "nests" or "bricks."

The second zone--here called the "reticular zone" on the basis of its cytoarchitecture--borders the relay zone continuously rostrally, ventrally, and caudally, thus enveloping it. It blends and interdigitates with the relay zone along their common border and blends even more gradually with the surrounding reticular matter of the brainstem. The reticular zone extends approximately 3.0 - 4.0 mm. rostrally from the rostral termination of the relay zone and approximately 1.0 - 2.0 mm. caudally from its caudal termination. It penetrates to a depth of approximately 1.8 - 2.0 mm. It contains smaller, 8.5 X 1.2 micron

cells which are irregularly shaped, but often triangular. These cells possess long but sparsely elaborated dendrites, giving them a "fusiform" appearance. Cells in this zone are less densely packed than in the relay zone (Basbaum & Hand, 1973; Berkeley, 1975; Berman, 1968; Hand, 1966; Hand & Lui, 1966; Keller & Hand, 1970; Kuypers, 1958a, 1958b; Kuypers & Hoffman, 1961; Kuypers & Tuerk, 1964; Kuypers, et al., 1961; Lund & Webster, 1967; Rustioni & Macchi, 1968; Rustioni & Sotelo, 1974; Taber, 1961).

3.2.2 Dual Modality Representation

Though fibres sensitive to both cutaneous and kinesthetic stimulation enter the DC, only the rapidly adapting cutaneous and a few of the most rapidly adapting kinesthetic fibres are present at cervical levels in the cat and monkey (Uddenberg, 1968a, 1968b; Whitsel, et al., 1969, 1970, 1972). In these species the slowly adapting fibres leave the DC before cervical levels and ascend via the dorsolateral fasciculi; most notably the spinocervical tract, from which they provide inputs to the DCN (Petit, 1972; Rustioni, 1973, 1976; Rustioni & Molenaar, 1975).

These DC and DC-dorsolateral fibres project to the relay and reticular zones respectively. Specifically, the realy zone in the cat receives a high concentration of hair-sensitive and light pressure inputs (Gordon & Jukes, 1962, 1964a; Kuhn, 1949; Perl, et al., 1962; Petit, 1972; Winter, 1965). Although the reticular zone contains units sensitive to such stimulation, they are present in fewer numbers (Gordon & Jukes, 1962, 1964a; Perl, et al., 1962; Rosen, 1967; Winter, 1965). Cat claw movement units appear only in the relay zone (Gordon &

Jukes, 1964a).

Although the relay zone of the cat contains a few cells responsive to kinesthetic stimulation, units signalling joint position and muscle spindle activation are more common in the reticular zone (Perl, et al., 1962; Rosen, 1969; Rosen & Sjolund, 1973; Winter, 1965). Mass potentials evoked by hair displacement and light touch in the DCN of cats are found at minimum amplitude in the reticular zone (Andersen, et al., 1970; Kuhn, 1949).

Most units in the cat relay zone respond to only one type of peripheral stimulation. On the other hand, many reticular zone cells are excited polymodally (Galindo, et al., 1968; Gordon & Jukes, 1962, 1964a; Kostyuk & Skibo, 1969; Rosen, 1967, 1969).

3.2.3 Dual Somatotopic Organization

Electrophysiological and histological data show that though both the relay and the reticular zones of the cat and rat display somatotopy along the classical lines (sec. 2.1), the body representation in the relay zone is specific and discrete, with little overlap of body segments. Representation in the reticular zone is comparatively diffuse and overlapping (Basbaum & Hand, 1973; Gordon & Jukes, 1962, 1964a; Hand, 1966; Keller & Hand, 1970; Kuhn, 1949; Winter, 1965).

Cells of the cat and rat relay zone are sensitive only to ipsilateral stimulation while reticular zone cells often have bilateral receptive fields (Blum & Whitehorn, 1973; Gordon & Jukes, 1964a; Gordon & Paine, 1960; McComas, 1962, 1963).

Some workers have found that the receptive fields of relay zone cells in the cat and rat are smaller than those of reticular zone cells

(Blum & Whitehorn, 1973; Gordon & Jukes, 1962, 1964a; Gordon & Paine, 1960; Gordon & Seed, 1960; McComas, 1962, 1963). Other workers have asserted that this apparent differentiation on the basis of receptive field size is actually a by-product of the fact that the more heavily innervated distal limbs project more densely and with smaller receptive fields upon their areas of representation in the DCN than do the less heavily innervated proximal limbs (Gordon & Horrobin, 1967; Kruger, et al., 1961; Perl, et al., 1962; Winter, 1965; Woudenberg, 1970). Whatever the reason for this differentiation of receptive field size in respect of DCN location, the fact remains that the dense, small receptive field innervation of the distal limbs projects to a well-defined area within the DCN. It will be recalled that this dense, small-field innervation is one of the properties of the classical dorsal column system held responsible for fine discrimination (sec. 2.1). The idea that such innervation is characteristic of the classical pathway finds support from the fact that DC lesion in cats reduces the number of units with small, sharply defined receptive fields which may be recorded in the DCN (Dobry & Casey, 1972b).

3.2.4 Dual Firing Characteristics

The absolute sensitivities to natural stimulation of relay zone units in the rat are typically higher and less variable than those of reticular zone cells (McComas, 1962, 1963). Units of the relay zone is the cat and rat usually display mutual inhibition while in the reticular zone mutual facilitation is often found (Gordon & Jukes, 1962; Gordon & Paine, 1960; Gordon & Seed, 1960; McComas, 1963; Perl, et al., 1962).

Average response latencies in the reticular zone of the cat and rat are longer, indicating more polysynaptic activation than in the relay zone whose response latencies suggest that monosynaptic activation predominates (Blum & Whitehorn, 1973; Gordon & Jukes, 1964a; Gordon & Seed, 1960; Kostyuk & Skibo, 1969; McComas, 1962, 1963). DC lesion in the cat reduces the proportion of cells with short latencies (Dobry & Casey, 1972b). Thus this property of relay zone cells appears to be characteristic of the classical pathway.

Units of the cat relay zone adapt more rapidly to continuous stimulation than do units of the reticular zone (Andersen, et al., 1970; Gordon & Jukes, 1964a; Perl, et al., 1962; Petit & Burgess, 1968).

3.2.5 Dual Descending Influences

Descending influences on the DCN presumed to be involved in motor functioning have already been summarized (sec. 2.4.4). These influences may be differentiated on the basis of their terminations within the DCN.

Lesions to the motor cortex in the cat produce paths of preterminal degeneration ending in the reticular zone of the contralateral DCN (Kuypers, 1958a; Kuypers & Hoffman, 1961; Kuypers & Tuerk, 1964; Walberg, 1957). Almost identical findings have been obtained with human material (Kuypers, 1958b).

Post-cruciate electrical stimulation in the cat inhibits cells of the DCN which show surround inhibition and excites those which display surround facilitation (Gordon & Jukes, 1963, 1964a). The inhibited cells lie primarily in the relay zone while the facilitated cells are found in the reticular zone.

Other work with cats indicates that the cortical effects, both inhibitory and facilitory, are distributed primarily to the reticular zone (Winter, 1965). Harris, et al., (1965) obtained similar findings with monkeys. In the monkey over 90 per cent of all units subject to cortical influence, either inhibitory or facilitory, are found in the reticular zone. Most of the cortically influenced units have large receptive fields while almost all of the unaffected units have small ones.

Thus, while it is unclear whether or not substantial cortical influences are delivered to the relay zone, those which have been detected are inhibitory. This is consistent with the predominantly inhibitory cortical effect on cutaneous units (sec. 2.4.1) which are located primarily in the relay zone (sec. 3.2.2). The fact that cells in the reticular zone which are inhibited by cortical stimulation have large receptive fields suggests that they are not part of the classical lemniscal pathway. It is clear from both the electrophysiological and histological studies that the corticonuclear influences implicated in motor functioning project more heavily to the reticular zone.

Stimulation of the reticular zone is more effective than stimulation of the relay zone in eliciting antidromic responses from the pontine reticular formation (Sotgiu & Cesa-Bianchi, 1976). This region is well known for its involvement in motor activity (Siegel & McGinty, 1977). This connection has also been histologically identified (Sotgiu & Marini, 1977).

3.2.6 Dual Efferent Connections

Many of the already described projections of the DCN (sec. 2.1;

sec. 2.4.1) arise preferentially from either the relay zone or the reticular zone.

While in the rat and the cat both cutaneous and kinesthetic modalities project by way of the ML to the VPL from both the reticular and relay zones, the cutaneous monosynaptic projection from the relay zone is the most massive (Berkeley, 1975; Boivie, 1974; Gordon & Horrobin, 1967; Gordon & Jukes, 1964a; Gordon & Paine, 1960; Gordon & Seed, 1960, 1961; Hand & Lui, 1966; Hand & Van Winkle, 1975; Lund & Webster, 1967; Rosen, 1967, 1969). On the other hand, though there is some overlap in zone of origin, projections to nonspecific thalamic and motor control areas (sec. 2.4.1) arise primarily from the reticular zone in the cat, rat, and monkey (Berkeley, 1975; Boivie, 1974; Bowsher, 1965; Gordon & Horrobin, 1967; Gordon & Seed, 1960, 1961; Hand & Lui, 1966; Hand & Van Winkle, 1975; Lund & Webster, 1967; Rinvik & Walberg, 1975).

3.2.7 Summary and Implications of Dual Organization

The DCN possess two cytoarchitecturally and functionally distinct subdivisions:

1. The first zone consists of large, densely packed, bushy cells which cluster together in discrete, shallowly overlapping areas of somatotopic representation. These cells respond to stimulation in single submodalities and have small receptive fields. They display mutual inhibition, low stimulus thresholds, short latencies, rapid adaptation, and high-frequency following. They receive their inputs primarily from first-order cutaneous DC fibres and project monosynaptically over the ML to the VPL. Whether or not they are modified by cortex is still at issue, but only inhibitory corticonuclear influences

have been identified. They are resistant to anesthetic effects. These properties are suggestive of a pathway which is able to encode and transmit rapidly and faithfully to cortex information about discrete and rapidly changing stimulus events on the skin. A description of classical dorsal column system cell properties (sec. 2.1) might well be substituted for a description of the cell properties of this zone. This zone is termed the "relay zone" because afferent impulses pass through its units on route to VPL rapidly and with a relative minimum of modification.

2. Cells in the second zone are fusiform rather than bushy, and sparsely distributed compared to relay zone cells. They display a fuzzy somatotopy and sometimes have bilateral receptive fields, unlike cells in the relay zone whose receptive fields are almost exclusively ipsilateral. They often respond in more than one modality and subtend larger receptive fields than relay zone cells. They often display mutual facilitation. Compared to cells in the relay zone their thresholds are high, their latencies long, their adaptation sluggish, and their following limited to low frequencies of stimulation. Cells in this second zone receive major kinesthetic inputs from tracts running in the dorsolateral funiculi. Most of these dorsolateral inputs are second or higher-order fibres. Though some of the cells in this zone send axons into the ML, these projections are often transsynaptic and frequently terminate in nonspecific thalamic nuclei as well as VPL. The extralemniscal projections to nonspecific thalamic nuclei and to brain-stem areas involved in motor function also arise from these cells. These cells also receive many more corticonuclear fibres than cells in

the relay zone and the influences descending via these fibres are both inhibitory and facilitory. Unlike cells in the first zone, they are easily anesthetized. This second zone is called the "reticular zone" because it possesses a cell morphology similar to that of the surrounding reticular matter of the brainstem.

The apparent functioning of the reticular zone is less clear-cut than that of the relay zone, but it appears to: (1) Integrate cutaneous and kinesthetic inputs. (2) Transmit such integrated information to cortical and brainstem areas responsible for the activation and control of motor sequences. (3) Transmit unintegrated kinesthetic information to cortex. This information is analyzed at cortex in respect of fine cutaneous information arriving over the classical DC pathway via the relay zone and VPL. (4) Allow cortical and brainstem feedback control over the afferent kinesthetic and cutaneous inputs generated by self-initiated motor activity and movement in general.

3.3 Summary and Experimental Hypotheses

DC lesions have not generally produced performance deficits in simple sensory tasks such as detection and gross localization. Deficits do appear, however, when sensory discrimination involves either active palpation of stimulus objects, or a passive recognition of subtle transformations produced at the skin by movement. This specific type of deficit suggests that at one or more higher levels in the brain kinesthetic information relevant to stimulus timing is integrated with cutaneous information relevant to stimulus place in such a way that

both are concurrently utilized in the detection of specific stimulus features. DC lesions may eliminate the capacity for judging the timing of cutaneous impingements generated by transformations of the body schema, or it may eliminate the source of these impingements; it may do both. The prevalence of motor disabilities following DC lesions suggests that cutaneous impingements are not adequately taken into account when motor sequences are executed.

Physiological and anatomical data suggest that afferent activity responsible for conscious appreciation of cutaneous stimulation, and afferent activity responsible for the integration of kinesthetic and cuntaneous inputs for their use in the formation of motor sequences, are transmitted by way of distinct anatomical substrates with the DCN. A region near the dorsal surface of the brainstem, just caudal to the obex, and only shallowly penetrating the brainstem, presents cellular functional features which suggest that it is a relay zone (RZ) for transmission of cutaneous information within the classical dorsal column system pathway. A zone of cells enveloping this relay zone, called the reticular zone (RTZ) because of its morphology of small, sparsely distributed cells, possesses features which suggest that it participates in motor functioning.

Thus Beck (1975, 1976a) has proposed that lesions of the RTZ, but not lesions of the RZ, should produce motor deficits of the type already described (sec. 2.4.2). (In Beck's papers, these zones are called the "rostral" and "caudal" zones respectively.) On the other hand, lesions

of the RZ should produce deficits in the sensory appreciation of differences caused by subtle movement. Corollary to Beck's proposals, if the ML is primarily an offshoot of the RZ, then transsection of this structure should have the same consequences as ablation of the relay zone.

For a first approach to these proposals, it was decided for this thesis to test for motor deficits following lesions of the RZ, the RTZ, and the ML. The specific hypotheses to be tested were: (1) RTZ lesions will produce deficits in animals' abilities to efficiently execute motor tasks which involve either locomotion in constrained circumstances or reaching for rapidly moving targets. (2) RZ and ML lesions will not produce such deficits.

The primary reason for choosing to test motor rather than sensory function in these first experiments in dual function was that motor deficits are easily observed. Motor tasks, which are extracted from the animal's normal repertoire of behavior, require much less special training and testing than do sensory tasks, if deficits are to be observed. Thus negative results in this study, i.e., motor deficits produced by lesions to the RZ or ML, or lack of motor deficits produced by lesions to the RTZ, would provide more information than negative results in sensory testing. Negative results in sensory testing, i.e, lack of deficit following any kind of lesion, would carry little information. Sensory deficits produced by DC lesion are not, at this stage, so well defined that their reproduction can be anticipated with any confidence. Lack of deficit following lesions may mean that an appropriate sensory task has not been selected, or it may mean that no

sensory deficit has occurred. In fact, no definitive statement about sensory function can be made with a lesion experiment until a sensory deficit has been obtained. (Other types of experiments will be dealt with in Chapter 6, the Discussion.) The difficulties in interpreting negative sensory data have already been discussed (sec. 2.3).

CHAPTER 4

METHODS

Had this study been carried out in its originally planned form, the effects of lesions on both acquisition and retention in motor tasks would have been studied. For acquisition, animals in all three lesion groups (RTZ, RZ, and ML) and a group of sham-operated controls would have been operated, trained to criterion, and then tested for post-criterion performance over a number of days. Measures of both acquisition and post-criterion performance would have been taken for each group and used for comparison purposes. For retention, animals would have been trained to criterion before surgery, tested for a number of days after attainment of criterion, operated, retrained to criterion, and retested. In addition to comparing performance among groups, each animal in the retention experiments would have served as its own control, in the sense that the magnitude of experimental effect for each animal could have been determined.

Unfortunately, due to several surgical failures early in the study, resulting in the deaths of animals after lengthy periods of pre-lesion training and testing, plans were changed. A continued high rate of surgical failure was anticipated, so plans to study retention, in all but one lesion group, were laid aside. Since the experimental hypothesis predicted that lesions to the RTZ should produce motor deficits, both retention and acquisition study was attempted for this lesion category only. It was reasoned that, should no deficit in performance be obtained (sec. 3.3), then the study of acquisition *vs* retention in all lesion categories would be superfluous to the purposes of this thesis. On the other hand, should the experimental

hypothesis be verified, pretraining and testing might mitigate the strength of the effect. Overtraining prior to surgery has been shown to reduce the strength of DC lesion effects in cats (Dubrovsky & Garcia-Rill, 1973).

4.1 Subjects

Subjects were 27 adult mongrel cats, 11 male and 16 female, 2.0 kg. to 4.4 kg. in weight, ranging in estimated age from seven months to four years. Animals were housed in individual cages in a colony room and maintained on dry laboratory feed and water when not being trained or tested.

Of the original 27 animals, 13 died during surgery or shortly thereafter. However, taking into account animals which were trained and tested prior to surgery, 17 cats, eight males and nine females, yielded behavioral data usable in some way. Six experimental groups were to be formed, depending on intended lesion manipulations and subject to histological verification of lesions: (1) Normal Controls: This group included six cats trained and tested before surgery, three of which died during or soon after surgery. (2) Sham-Operated Controls: This group consisted of three cats trained and tested after surgery. (3) RTZ Lesion Group I - Retention: This group was to contain three cats trained and tested both before and after surgery. (4) RTZ Group II - Acquisition: This group was to hold three animals which were trained and tested only after surgery. (5) RZ Lesion Group: This group consisted of four animals trained and tested after surgery. (6) ML Lesion Group: This group was to have four animals, trained and tested postsurgically.

4.2 Experimental Tasks

Cats are well known for their agility and precision in jumping, climbing, walking, balancing and reaching. They run rapidly on narrow branches in the pursuit of small, elusive prey such as voles and birds. They pounce on prey quickly with their forelimbs. The "game of cat and mouse," which cats often play once they have caught their prey, requires a good deal of paw dexterity. Cats have been observed to snare birds in flight from the air (Heckmann, 1971). Thus the two tasks selected from previous DC lesion literature were intended to tap a portion of this natural repertoire. One was a walking and balancing task (Melzack & Bridges, 1971). The other was a rapid reaching task (Dubrovsky & Garcia-Rill, 1973; Dubrovsky, et al., 1971). Cats with DC lesions do not perform in these tasks as well as do sham-operated or normal controls.

4.2.1 Walking and Balancing Task

In this task animals were required to walk along a wooden beam in order to obtain food reward. Their performance was evaluated in terms of errors made in stepping and turning while walking.

4.2.1.1 Apparatus. All animals trained and tested preoperatively walked on the edge of a narrow pine beam. This beam was 304.8 cm. long, 4.4 cm. wide on the walking surface, and 9.2 cm. deep. It was mounted sawhorse-style such that the walking surface was level and straight. The walking surface measured 149.9 cm. from the floor. On either side and at both ends of the beam, blocks were set in order to accommodate the sawhorse supports. There were eight of these in all, two on each side and at each end of the beam, mounted on the side

of the beam such that a 2 cm. slot existed between them for the insertion of the sawhorse supports. Each of the blocks was 9.2 cm. long, 9.2 cm. deep, and 4.4 cm. wide. The centers of slots formed by each set of four blocks measured 62.4 cm. from their respective ends of the beam. These blocks are described since they provided the animals with additional stepping surfaces.

Since several of the animals trained only postoperatively showed deficits severe enough that they could not be trained on the beam described above, all animals trained and tested only postoperatively walked on a wider beam. This beam was a 304.8 cm. X 9.5 cm. X 1.9 cm. board nailed on top of the original, narrower beam. Its thickness raised the walking surface up to 151.8 cm. from the floor. The dimensions of the walking surface of this wider beam were almost identical to those of the beam used by Melzack and Bridges (1971).

In order that estimates of scoring reliability might be obtained after testing had been completed, walking performance was recorded. A Panasonic 9177 black and white television camera was tripod mounted at one end of the beam. Its lens was set level with the top of the beam and focused down its length such that the footwork of animals was the predominant feature of tapes made of their walking behavior. Portions of walking performance were recorded on a Sony CV 2700 black and white video tape recorder using Scotch or Karex one half inch video recording tape. Recorded performance was viewed on an Electrohome ETV 3B.019 video monitor.

4.2.1.2 Training. Animals were maintained on 23 hour food deprivation during training and testing. On the first day of training

they were placed on the end of the beam nearest the television camera and allowed to feed on Heinz Beef With Broth baby food offered to them on a spoon. Animals that jumped off the beam were put back on, some repeatedly, until they would sit quietly and feed without attempting to jump. The bait was then held just out of reach and animals were coaxed to walk towards it by talking to them and tapping the spoon on the beam. They were occasionally encouraged by a push to the hindquarters. By gradually lengthening the distance the animals had to walk to be fed, they were shaped to walk from one end of the beam to the other without feeding in between.

Beginning at the end of the beam closest to the camera and facing the camera, an animal would turn, walk to the other end of the beam and be fed there, turn again and walk back to the camera end. This sequence was called one trial. After three successive days of walking for five successive trials, animals were considered trained. On subsequent days animals were tested and scored. Training procedure was the same on the narrow as on the wide beam and for preoperative training as well as postoperative training and retraining.

4.2.1.3 Testing and Scoring. Animals were tested ten trials per day for ten days in succession. They were scored for certain types of errors which preliminary observations had shown occur commonly but infrequently in normal cats. These errors were divided into four scoring categories: (1) Paw Slips: Slips of the paws, either off the sides of the beam once that they had been placed on the beam and the weight of the body had been rested on them, or along the beam in sliding, shuffling, or tripping motions, were scored as

Paw Slips. (2) Paw Placement Errors: These errors occurred when paws, apparently directed towards the beam as part of a step, missed the beam and went off into empty space. (3) Pivoting Errors: These were scored when discontinuities appeared in the usually smoothly executed sequence of rearing up on the hindlimbs, swinging the body around 180 degrees, and pointing it in that direction along the beam. Any loss of balance or misdirection of the body leading to errors in the other three classes, if made during a pivoting sequence, was scored as a Pivoting Error. (4) Falls: If animals either fell off of the beam completely or lost enough control such that portions of their bodies other than their feet impacted with the beam, Falls were scored. Falls were scored if they resulted from initial errors in any of the other three categories or if they occurred without apparent cause.

As such "errors" appear, albeit with low frequencies, in normal cats, some justification is needed in calling them errors at all. The animal is presumably attempting to reach the food bait as quickly and as efficiently as possible. There were some animals who would from time to time jump down off the beam and run about the experimental chamber. However, none of these animals, when the food reward was made available, chose to jump off the beam, run along the nearby table, and jump back up to take the bait. They always took the shortest route. Events of the type scored as errors interrupted otherwise smoothly continuing walking sequences, which continued on as before, after the interruption. They appeared to detract from the efficiency of the motor act directed at obtaining bait. Though to think in these terms

may be somewhat anthropocentric, the same interruptive events occurred with high frequencies in cats with DC lesions (Melzack & Bridges, 1971). Thus they are the kinds of events which the experimental hypothesis predicted would occur with increased frequencies after reticular zone lesions.

Following the example of Melzack and Bridges (1971), no more than one occurrence of a given error type was recorded in a given trial. Incidental observations were made of animals' individual styles of walking. Changes in style with practice and lesion were also recorded. All initial observations were made by the author.

Because of the somewhat subjective nature of scoring criteria, data required for estimates of inter-rater and rate-rerate reliability were obtained. A sample of the original trials, taken from performance of all animals under all conditions, was recorded on video tape and later rescored by the original experimenter and a semi-independent observer.

4.2.2 Reaching Task

The second task required that animals rear up on their hindlimbs to quickly reach out and either snare, or knock to the floor, a piece of meat hanging from the rim of a rapidly rotating wheel. This task was adopted directly from Dubrovsky and Garcia-Rill (1973) and Dubrovsky et al., (1971).

4.2.2.1 Apparatus. The central piece of apparatus was a 62.2 cm. diameter, 0.3 cm. thick, black plexiglass disc mounted vertically on a rotating shaft such that its lower edge was 71.4 cm. from the floor of the experimental chamber. The disc was rotated by means of

a Robins and Meyers one quarter horsepower, 115 volt, 60 cycle AC electric motor attached to a Zero-Max 30K400 reduction clutch drive with a variable speed control. This arrangement allowed the precise adjustment of rotational speed within the range of speeds used. A small, flexible spring was mounted on end near the outer edge of the disc, protruding outward toward the area in which animals were enclosed and in the opposite direction from the drive apparatus. A sharpened bolt was mounted in the free end of the spring such that its point also faced the animal enclosure. Though sharpened, this bolt was still blunt enough so that no animal ever injured itself. A small piece of Pride of Canada Brand Baloney was hung on this sharpened bolt as a reaching target.

A cardboard enclosure was constructed in order that animals might be confined to a limited area during reaching performance. The enclosure was 71.1 cm. long, 66.0 cm. wide, and 84.6 cm. deep. It was left open overhead. The disc was mounted within the enclosure such that its rear surface was 15.2 cm. from one of the narrower ends of the enclosure.

4.2.2.2 Training and Acquisition Scoring. Animals were maintained on 23-hour food deprivation during training and testing. Over a period of days they were habituated to the restraining enclosure and the sound of the drive motor. They were gradually enticed to reach higher and higher for bait dangled over their heads until they voluntarily took it from the bait hanger. At this point in training, the disc was stationary and the bait hanger rested at the rotational perigee of the disc. After animals grew used to taking the bait under

these conditions, rotation of the disc was begun. It was rotated slowly in early training, and more quickly as training progressed. During this period, animals were allowed 15 successful reaches a day. A successful reach consisted of either snaring the bait off of the bait hanger or knocking it to the floor. The first rotational speed recorded was 6 r.p.m. If the animal successfully reached four times in a row at any given rotational speed, the speed was advanced 2 r.p.m. Speed was thus increased by 2 r.p.m. increments until animals had reached the training criterion speed of 20 r.p.m. Any given training period was discontinued if an animal failed to reach for bait for three consecutive minutes before its permitted 15 successful reaches per day had been attained. When animals had made at least 15 attempts per day for three days in a row, they were considered trained and testing began the next day.

In order that acquisition in the reaching task might be compared across groups, the number of attempts (trials) required to reach training criterion for each animal were recorded.

4.2.2.3 Post-Criterion Testing and Scoring. Behavioral testing continued for ten days after criterion had been attained. Animals were allowed 20 successful reaches per day during this period for a total of 200 trials per animal. Three parts of the motor sequence involved in successfully reaching for the bait and finding it once it had fallen to the floor were scored according to the scheme of Dubrovsky and Garcia-Rill (1973) and Dubrovsky, et al., (1971):

1. Efficiency of the reach was evaluated as the percentage of successful releases of bait from the bait holder, per number of

attempts, without taking into account the precision of execution of the reach.

2. Accuracy was expressed as the frequency (total number) with which animals hit the holder instead of the target, failing to release the bait, i.e., an animal was less accurate the more it hit the holder without releasing bait.

3. Tracking of the released bait in space, considered a measure of an animal's ability to oreint its body to the visually appreciated trajectory of the released bait, was assessed by counting the times the animal localized it within three seconds after it had been released. The fact that the bait was mounted on a spring resulted in many different and often bizzare trajectories once it had been released, rather than a simple vector determined by the reach of the animal and the pull of gravity. Thus an animal's ability to orient its body in respect of the trajectory of released bait was an important factor in its quick localization on the floor. When animals snared the bait and carried it directly to the mouth, this was scored as zero latency.

Over the first five days of testing the speed of the disc was advanced 2 r.p.m. per day, such that by the sixth day it rotated at 30 r.p.m. It remained at this speed for the last five days of testing. Thus the final disc speed was close to the 34 r.p.m. speed used by Dubrovsky and Garcia-Rill (1973) in similar experiments. As with the beam task, incidental observations on individual performance styles were recorded.

4.3 Surgical Procedures

4.3.1 General Procedures

Animals were food and water deprived for 16 hours prior to surgery. Because surgery did not take place under strictly aseptic conditions, a high circulating level of antibiotic was ensured for the time of surgical incision by intramuscular administration of 10 mg./kg. chloramphenicol (Rogar-Mycine 200, Rogar STB) when food and water deprivation was begun. This dosage was repeated just after surgical anesthetic had been given. On the morning of surgery animals were anesthetized with 38 mg./kg. pentobarbital (Diabutal, Diamond Laboratories), administered intraperitoneally. When anesthesia deepened to the point that flexion withdrawal of the forelimb could not be elicited by a firm pinch between the toes, the head of the animal was shaved and disinfected. The animal was then placed on the surgical table with its head in a stereotaxic frame. Artificial warming was begun at this time, by means of a heating pad between the cat and the surgical table. Rectal temperature was maintained at 37±1 centigrade throughout surgery.

Separate surgical procedures for obtaining physiological control data and for the four different lesion conditions are described below.

4.3.2 Physiological Control Procedures

Forebrain potentials elicited by subcutaneous electrical shock stimulation to the contralateral forelimb were used as a measure of the continuity of transmission in the lemniscal pathway before, during, and after lesioning, and at the time of the sacrifice.

The skin between and slightly above the orbits was incised along

the midline and retracted. The underlying fascia was blunt dissected, exposing the skull overlying the frontal sinuses. A small hole was drilled unilaterally just rostral of the border of the area of dense bone vascularization denoting underlying brain tissue. This small opening into the frontal sinus was enlarged by gnawing the surrounding bone with fine rongeurs until the bony wall separating the frontal sinus from the brain was clearly exposed. A minute hole was drilled into this wall with a pin vise using a 1.0 mm. bit. This hole was placed about 4.0 mm. lateral to the septum of the sinus and about 4.0 mm. ventral to the junction between its roof and caudal wall. Thus the hole was located approximately above the forelimb projection area of the post-sigmoid gyrus. This location was well suited for recording evoked lemniscal potentials. The hole was not drilled completely through the bone, but a small recording screw, which also did not penetrate the bone, was fastened into it. A similar screw was inserted as an indifferent electrode into the bone on the dorsal surface of the skull at the midline, just caudal to the junction of the septum and caudal wall of the frontal sinus.

Evoked potentials, post-sigmoid area negative, were recorded between the two screws using Tektronix P6062A Passive Probes attached to a Tektronix R5031 Dual Beam Storage Oscilloscope. The oscilloscope was triggered by a Grass Instruments S88 Stimulator which at the same time provided the shock stimulus pulse. Shock pulses were rectangular monophasic waves of varying amplitudes, but none exceeding 20 volts. Pulse width was 5.0 msec. and pulse frequency was varied from 1/sec. to 10/sec. Pulses were delivered to subcutaneous needle electrodes

in the dorsal aspect of the forelimb contralateral to the recording site. They were fed through a Grass Instruments SIU5 Stimulus Isolation Unit.

Before lesion surgery began, "normal" brain activity evoked by shock stimulation and recorded on the oscilloscope was studied. Photographs were made of several stored, superimposed records of cortical activity obtained both with and without shock stimulation. Photographs were taken using a Tektronix C70 Oscilloscope Camera loaded with Polaroid Type 107 black and white film.

Evoked potential activity could not be recorded in some animals due either to proliferation of bony growth throughout the frontal sinuses making placement of recording screws impossible, or due to failure to locate an evoked potential after several screw penetrations. In such cases lesions were placed without benefit of the evoked potential control.

During the course of lesioning, evoked potential activity was studied in order to control lesion extent. The features of evoked potential changes which were used in controlling lesions varied among the lesion types. Thus specific details relevant to these features are given in the appropriate procedural sections on lesioning below.

After lesions were judged complete on the basis of evoked potential activity changes and visual inspection of the lesions, photographs were again made of superimposed oscilloscope traces obtained both with and without shock stimulation. Recording screws were then extracted and the holes plugged with sterile bone wax. Any fluid remaining in the frontal sinus was then greatly aspirated through a

blunted, 20 ga., 1 1/2 in. hypodermic needle by means of a J. Sklar Mfg. Co. 100-65 suction device operating at a pressure of 10 mm. mercury. The inside of the sinus was sprinkled with antibiotic powder (Eye and Wound Powder, Ayerst). A piece of opthalmic Gelfilm (Upjohn) was cut to fit and placed over the opening in the bone over the frontal sinus. The skin was then sutured back into place.

At the time of sacrifice, usually several weeks following initial surgery, the animals on which evoked potential data had been obtained were given a normal dose anesthetic and the frontal sinus over the recording site was reopened: The stimulating, recording, and photographing procedure was repeated. After this, the lethal anesthetic dose was administered. These terminal experiments sought to establish whether any recovery in evoked potential activity had taken place in lesioned animals, and had thus paralleled any behavioral recovery of deficits.

4.3.3 Dorsal Column Nucleus Lesions

After completion of pre-lesion control recordings, lesion surgery began. In order to secure maximal separation of the dorsal aspects of the atlas and the occipitus, the head of the animal was flexed forward, being pivoted on the stereotaxic earbars, and confined in this position. The skin was incised caudally for about one inch from the dorsal aspect of the external occipital ridge along the midline of the dorsal surface of the neck. The skin was retracted and successive layers of muscle and fascia were incised along the midline aponeurosis. This was done by inserting the point of the scalpel blade, cutting edge downwards, under a given layer where it met the occipitus, and then

tugging sharply upwards with the blunt edge of the blade. This technique left the muscle attachments to the skull intact and led to no excessive bleeding from muscles and fascia. Aside from being less traumatic, it was quicker, in terms of time needed to penetrate all muscle layers and expose the dura, than blunt dissection of muscle attachments at the occipitus, a technique tried on the first two animals operated. Each succeeding layer of muscle was retracted until the dura was visualized, stretched and exposed, between the atlas and the occipitus. The fatty tissue adhering to the dorsal surface of the dura mater was gently scraped away until the underlying brainstem could easily be visualized. At this point, with the head flexed forward, the tip of the cerebellum and the caudal apex of the fourth ventricle were usually visible just rostral of the foramen magnum.

Since from this point on different surgical procedures were used for RZ and RTZ lesioning, these procedures are presented separately below.

4.3.3.1 Relay Zone Lesions. The exposed dura was longitudinally incised caudad from its attachment to the foramen magnum for about 7.0 mm. along the midline of its dorsal aspect. After cerebrospinal fluid had stopped flowing, the caudal apex of the fourth ventricle was visualized, sometimes directly, sometimes by pressing the cerebellum upwards into the skull with a narrow spatula. Beginning just behind this point and continuing for about 4.0 mm. caudally, the pia mater was gently dissected away with a fine forceps laterally to the extent of the dorsolateral sulcus. A Carl Zeiss 48009 dissecting

microscope, set at a magnification of 16 x, assisted in this procedure. Also with the help of the microscope, the neural tissue underlying the pia mater dissection was gently torn with fine forceps and aspirated with approximately 3.0 mm. mercury suction (see sec. 4.3.2 for suction device and suction tip). This RZ lesion was made to a depth of approximately 1.0 mm. to 1.5 mm. During the lesioning procedure, evoked potential activity was observed at frequent intervals. If a dramatic decrease in potential amplitude was observed at any point in the process, the RZ lemniscal pathway was considered severed and lesioning was ceased. A large decline, but not a complete disruption, in evoked potential activity was sought. This was because cellular elements of the RZ and RTZ overlap and excessive incursion into the RTZ was not desired, even at the cost of allowing some lemniscal activity to remain intact. Care was taken during the lesioning process to keep the appearance of lesions symmetrical, since lesioning took place bilaterally and evoked potential control was only unilateral. Figure 1 presents a diagram of the RZ lesion placement.

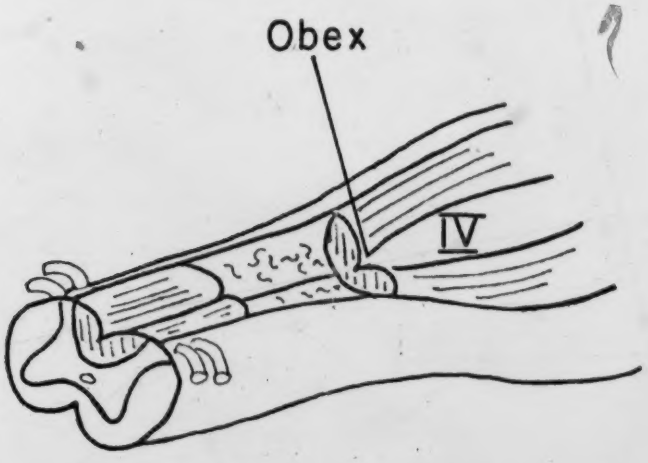

Figure 1. Relay Zone Lesion Placement

After the lesion had been made and bleeding from the traumatized area had stopped, clotted blood was gently aspirated out of the subdural space. The flaps of dura mater were then reopposed with a No. 7 silk suture attached to a G-6 cutting needle (Ethicon). The needle for the dura suture was driven with a Castroviejo Needle Holder with Catch (Hartz, cat. No. BM 563). A piece of Gelfilm was cut to fit and inserted under the atlas and over the occipitus, thus covering the often imperfectly reapproximated dural flaps. Antibiotic powder was sprinkled into the wound and the muscle layers were reapproximated with catgut sutures. Antibiotic powder was sprinkled into the wound after each layer of wound closure. The skin was reapproximated with silk sutures.

4.3.3.2 Reticular Zone Lesions. Surgical procedure was the same as for RZ lesions up to the exposure of the dura mater. Since most of the volume of the RTZ lies rostral to the RZ, it was decided that the most effective lesion would be to the obex (see Figure 2).

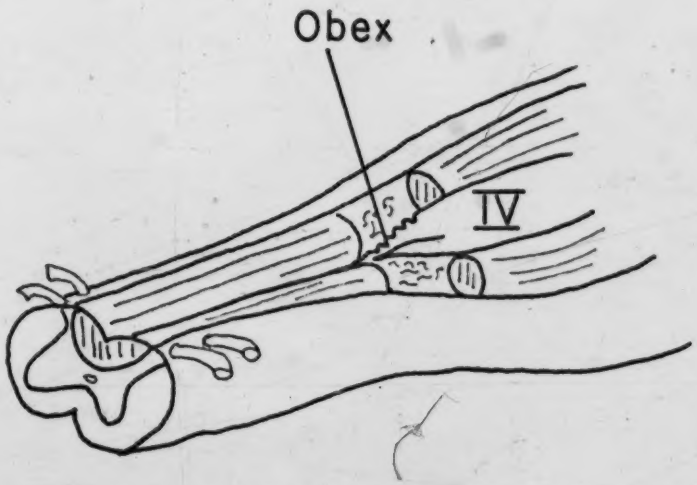

Figure 2. Reticular Zone Lesion Placement

The attachments of the dura to the skull at the foramen magnum were carefully scraped away. This left the dura free of the edge of the foramen magnum but still intact over the brainstem. The foramen magnum was then enlarged dorsally and laterally by gnawing the bone away with fine rongeurs until the cerebellum could be elevated with a narrow spatula enough to expose the brainstem to the reach of instruments for about 5 mm. rostral to the obex.

An electrolytic lesion technique was attempted in the first three RTZ animals. Electrodes were 000 ga. stainless steel insect pins (Elephant Brand), insulated except for 1.0 mm. at the tip with Insul-X Insulating Tool Dip. These insect pin electrodes were soldered into 000 ga. stainless steel tubes. The tube and pin electrode apparatus was manipulated into place using a David Kopf Instruments stereotaxic manipulator. The first electrode penetration was made such that the electrode tip rested at a depth of 1.2 mm. in the brainstem, 1.0 mm. rostral of the obex, and 1.0 mm. lateral to the lateral wall of the fourth ventricle. A 40 second, 30 milliampere DC current was passed between the electrode and an alligator slip on the ear of the animal, electrode positive. A C. H. Stoelting Co. 58040 Lesion Generating Device generated the current. Such a current had previously produced 1.5 mm. diameter coagulation in raw egg white and the same size lesion in formalin-fixed cat brain tissue. Thus it was presumed that the same size lesion would be accomplished in the brainstem of the living cat. Similar lesions were placed 1.2 mm. laterally, 1.2 mm. rostrally, and 1.2 mm. rostrally and laterally of the first lesion, for four lesions in all on one side of the brainstem. The procedure was

repeated on the other side of the brainstem for a bilateral lesion. Only one animal on which this procedure was attempted survived surgery. The other two died on the operating table soon after the lesions had been made, apparently of respiratory failure.

Subsequent RTZ lesions were attempted with two different techniques. The first of these was mechanical dissection after the manner of RZ lesion, but with the cerebellum elevated as with the electrolytic lesions so as to expose the RTZ (sec. 4.4.3.1). However, out of eight animals in which this procedure was attempted, four expired shortly after lesioning or within two days after recovery (see sec. 5.1). Histology showed that the remaining four either had lesions placed too shallowly or too far caudally to affect the RTZ (see sec. 5.2).

The second attempted alternative procedure utilized a variation on a thermocoagulation technique first presented by Dusser de Barenne (1935) and modified by Heimer and Lohman (1975). A 3 mm. diameter brass bar was fitted as a probe tip to a Ron-Kote 25 w. soldering iron. The end of the tip was hammered down to a flat plate 0.5 mm. in thickness. The flat portion of the bar, which was 1.0 cm. in length, was then ground to the shape of the dorsal surface of the rostral portion of the DCN on one side of the brainstem. The heat output of the soldering iron tip was regulated by a "Powerstat" variable resistor (Superior Electronics Co.). The heat output of the soldering iron was calibrated to the dial settings of the Powerstat by means of a YSI 42SF Tele-Thermometer. Though no direct information relevant to thermocoagulative lesions in the cat brainstem

could be located, it was estimated on the basis of the depth of lesions of the cortex in other animals produced by a similar technique (Dusser de Barenne, 1933; Heimer & Lohman, 1975), that the heat necessary to achieve the desired lesion of the RTZ, but not sufficient to destroy underlying structures, is approximately 70 Centigrade degrees applied for from three to five seconds. With the cerebellum elevated, this intensity and duration of heat was applied to the brainstems of five animals. Of these, one survived (see sec. 5.1) long enough to be tested. The others died in surgery or soon after.

Evoked potential activity was monitored periodically during lesioning, as with RZ lesions. But since no interruption of lemniscal transmission was anticipated or desired in the case of RTZ lesions, lesioning was halted if any decrement in evoked potential amplitude was observed. As with RZ lesions, care was taken to keep tissue damage bilaterally symmetrical. Closure of the surgical wound was the same as with RZ animals, with the addition that the traumatized bone around the foramen magnum, which showed a tendency to bleed profusely, was stopped up with bone wax.

4.3.3.3 Sham-Operated Controls. Since maximal surgical trauma, short of actual lesioning, was desired in the sham-op animals, procedure was the same as for reticular zone animals, including elevation of the cerebellum and gentle mechanical manipulation of the brainstem. The only exception was that brainstem neural tissue was not destroyed. Evoked potential control data was obtained as with lesion groups.

4.3.4 Medial Lemniscus Lesions

A stereotacic electrolytic technique was utilized in order to

bilaterally interrupt the ML caudal to its termination in the VPL. Stereotaxic coordinates for this purpose were taken from Snider and Nieman (1961).

For these lesions the head of the animal was not flexed, but fixed in the "zeroed" stereotaxic position. The coronal surface of the skull was exposed and holes were drilled bilaterally at the appropriate coordinates. These holes were enlarged mediolaterally with fine rongeurs in order to allow mediolateral variation in electrode insertion. The dura beneath these openings was incised to allow easy electrode penetration.

Rather than relying solely on stereotaxic corrdinates for lesion placement, a control procedure taking advantage of evoked ML potentials was used in order to locate and map out the ML for lesioning and to verify lesions. An insect pin electrode (constructed and manipulated as in sec. 4.3.3.2) was lowered into the area of the brain where stereotaxic coordinates indicated the ML should be. In successive mediolateral electrode penetrations, lemniscal evoked potentials in response to subcutaneous forelimb shock (sec. 4.3.2) were explored. The cross-section of the ML was graphically outlined by noting the dorsal-ventral extent of maximum evoked potential amplitude at each mediolateral penetration. When the ML cross-sectional area had been mapped, a 15 milliampere DC current, 30 seconds in duration, was passed between an electrode tip placed in the center of the mapped area and a stainless steel anal probe, the electrode positive. Such a current had previously been shown to produce 1.8 mm. diameter lesions in perfused, but unfixed, cat brain tissue. The evoked potential was

checked with a fresh electrode throughout the mapped-out ML area in order to determine the completeness of the lesion. This procedure was performed bilaterally.

In addition, the usual evoked potential control was performed (sec. 4.3.2). Moreover, it was performed bilaterally, since the area lesioned was not open to visual inspection for bilateral symmetry of lesions.

After lesions were complete, the openings in the skull were filled with dental acrylic (Formatray, Kerr). The skin was sutured back into place.

4.3.5 Surgical Recovery

After surgery, animals were removed from the stereotaxic frame, injected with another dose of antibiotic, and placed in warmed fibre-glass recovery cages in an isolation room. Antibiotic administration continued, in two half-daily doses per day, for four days following surgery. While animals were still unconscious, the side on which they lay was frequently changed in order to minimize lung congestion and bedsores. During this same period their mouths were kept wet with water dripped from a syringe. After regaining consciousness, most animals refused solid food for about a week. During the first few days, the most seriously debilitated animals were unable to move about their cages and get food for themselves. For these reasons most animals were hand-fed water and pureed beef baby food through a syringe. Daily observations of body weight, muscle and reflex tone, and placing, righting, support, and withdrawal reflexes were made. When animals were able to sit up and move about, they were returned

to their home cages. Observations of reflexes continued. Animals were considered recovered and ready for postoperative training when they had begun voluntarily to take solid food, their weight had steadily begun to rise, and they attempted to move about the cage and play with the experimenter as they had done before surgery.

4.4. Histology

Histological examination was undertaken in order to verify lesion location and extent. Immediately after the terminal control experiments (sec. 4.3.2), animals were killed with an overdose of 76 mg./kg. pentobarbital. They were perfused through the heart with 0.09 per cent saline and the upper body was fixed with 10 per cent formalin. Brains and upper cords were removed from the animals and preserved for at least one week in 10 per cent formalin. Portions of brains containing lesions were dehydrated, embedded in parrafin, and sectioned serially in 15 micron frontal sections. Sections at intervals of about ten sections were mounted on microscope slides and deparrifinated. Of these, every other section was stained with Luxol Fast Blue myelin stain. The remaining sections were stained with a modified (Hammond, in preparation) Cresyl Violet nissil stain.

CHAPTER 5

RESULTS

Table 1 summarizes the surgical and training procedures to which animals were submitted. Animals are listed in chronological order for date of surgery.

Of the 27 animals used in this study, 14 survived surgery long enough for some postoperative data to be obtained. Of the six animals in which RZ lesions were attempted, one (C-16) died from internal bleeding over the lesion site while another (C-18) succumbed to infection. RTZ lesions were attempted in 14 animals. Of these, four survived, while the others died of various causes (sec. 5.1.2).

Note in Table 1 that four animals were tested postoperatively in the walking task but not the reaching task. Training difficulties were responsible in two cases (C-7, C-49). In the other two cases (C-118, C-203) the animals were blind postoperatively (sec. 5.1.1.6).

Evoked potential records were not obtained from three animals (C-18, C-52, C-16), as suitable recording sites could not be located.

To summarize, useful behavioral data was obtained from 17 animals. Of these, 14 survived long enough to be tested postoperatively. Eleven of these 14 received training only after surgery and formed the acquisition condition in these experiments. The three remaining animals formed the retention condition. All 17 animals performed in the walking task. Thirteen animals performed in the reaching task, two in the retention condition and eight in the acquisition condition. Three of the animals which died during or shortly after surgery, but were preoperatively trained and tested, formed part of a normal control

Table 1

Synopsis of Obtained Data

Subject	Date of Surgery	Survival Time	Recovery Time	Walking Pre-Op	Walking Post-Op
C-7	27/6/76	64 d.	21 d.	+	+
C-18	24/8/76	10 d.	———	+	-
C-16	25/8/76	2 d.	———	+	-
C-30	6/10/76	0 d.	———	+	-
C-53	13/10/76	90 d.	24 d.	-	+
C-52	15/10/76	81 d.	26 d.	-	+
C-51	20/10/76	98 d.	19 d.	-	+
C-50	26/10/76	3 d.	———	-	
C-49	3/11/76	73 d.	22 d.	-	+
C-35	5/11/76	64 d.	19 d.	+	+
C-20	6/11/76	69 d.	18 d.	+	+
C-90	4/12/76	0 d.	———	-	-
C-86	6/12/76	65 d.	28 d.	-	+
C-117	18/1/77	65 d.	26 d.	-	+
C-104	19/1/77	0 d.	———	-	-
C-116	21/1/77	67 d.	25 d.	-	+
C-119	5/2/77	6 d.	———	-	-
C-118	25/2/77	76 d.	20 d.	-	+
C-153	26/4/77	64 d.	26 d.	-	+
C-203	27/4/77	76 d.	28 d.	-	+
C-45	25/8/77	0 d.	———	-	-
C-9	26/8/77	0 d.	———	-	-
C-41	27/8/77	1 d.	———	-	-
C-46	28/8/77	0 d.	———	-	-
C-38	1/9/77	6 d.	———	-	-
C-125	6/9/77	45 d.	15 d.	-	+
C-24	7/9/77	2 d.	———	-	-

+ data obtained

- no data obtained

Table 1

Synopsis of Obtained Data (Continued)

Reaching Pre-Op	Reaching Post-Op	Intended Lesion	E. P. Control	Intended Lesion Obtained
-	-	RTZ Elec.	+	-1
+	-	RZ	-	+
+	-	RZ	+	+
+	-	RTZ Elec.	+	2
-	+	RZ	+	+
-	+	RZ	-	+
-	+	RZ	+	+
-	-	RTZ Mech.	+	+
-	-	RZ	+	+
+	+	RTZ Mech.	+	-1
+	+	RTZ Mech.	+	-1
-	-	RTZ Elec.	+	2
-	+	Sham-Op	+	+
-	+	Sham-Op	+	+
-	-	RTZ Mech.	+	+
-	+	Sham-Op	-	+
-	-	ML	+	+
-	-	ML	+	+
-	+	ML	+	+
-	-	ML	+	+
-	-	RTZ Mech.	+	+
-	-	RTZ Mech.	+	+
-	-	RTZ Heat	+	+
-	-	RTZ Heat	+	+
-	-	RTZ Heat	+	+
-	+	RTZ Heat	+	+
-	-	RTZ Heat	+	+

1 but assignable to a lesion group
2 histological data unavailable

group (sec. 5.1.1.1).

5.1 Histological and Evoked Potential Controls

The primary objective of this thesis was to compare the effects of RZ and RTZ lesions on retention and acquisition in certain motor tasks. However, only three of the six originally planned experimental groups (sec. 4.1) were obtained in their intended numbers. Specifically, after histological verification of lesions, only the Normal Control Group (N = 6), the Sham-Operated Control Group (N = 3), and the RZ-Lesioned Acquisition Group (N = 4) were obtained in full numbers. One of the four animals which survived attempted RTZ lesioning presented a verified lesion in this zone. This animal participated in the acquisition condition. Of the remaining three surviving attempted RTZ preparations, all in the retention condition, two showed only minor damage limited to the fibre tracts overlying a zone of cytoarchitectural transition between the RZ and the RTZ. The other animal presented deeper damage, involving both fibre tracts and nuclear material, at the same level. Three out of the four attempted ML preparations survived and showed verifiable ML damage.

The original numbers in each group were chosen in order to fulfill certain requirements for statistical testing of prior hypotheses. As the number of animals in some groups fell short of those required, certain of the originally planned statistical tests could not be made. This and related problems will be taken up below (sec. 6.2).

The next section (sec. 5.1.1) describes in some detail the histological findings noted above. Since study of certain lesion and technical factors is of some interest in explaining (and in the

future, hopefully preventing) the high death rate among attempted RTZ preparations, the second following section (sec. 5.1.2) will present the histological findings for non-surviving RTZ animals.

5.1.1 Lesion Verification and Assignment to Groups

5.1.1.1 Normal Controls and Sham-Operated Controls. The first group, that of six Normal Control animals, consisted of animals trained and tested prior to surgery. The brainstems of these animals are presumed to be similar to those of two of the three Sham-Operated control animals (C-116, C-117), which showed no apparent tissue damage. Thus Figure 3a., a composite reconstruction of the histology of C-116 and C-117, is taken to represent the appearance of a Normal Control animal's brainstem as well.

This illustration, and subsequent brainstem lesion reconstruction illustrations, are accompanied by a representation of relevant pre-lesion and post-lesion evoked potential records, with time and amplitude scales as indicated. The histological reconstructions themselves represent 15 micron thick frontal sections, spaced at 0.5 mm. intervals. These sections pass at some point through the level of the obex, which is indicated by an arrow. Lesioned areas are stippled. Thus the reconstruction in Figure 3a. represents the brainstem from 5.0 mm. caudal of the obex up to 4.0 mm. rostral of the obex. Nearly the full extent of the DCN is thus included in the diagram, and no damage shows.

The third Sham-Op animal, C-86 (Fig. 3b.) displayed a shallow and sparsely elaborated margin of gliosis on the dorsal surface of the brainstem. This began at the level of the obex and extended

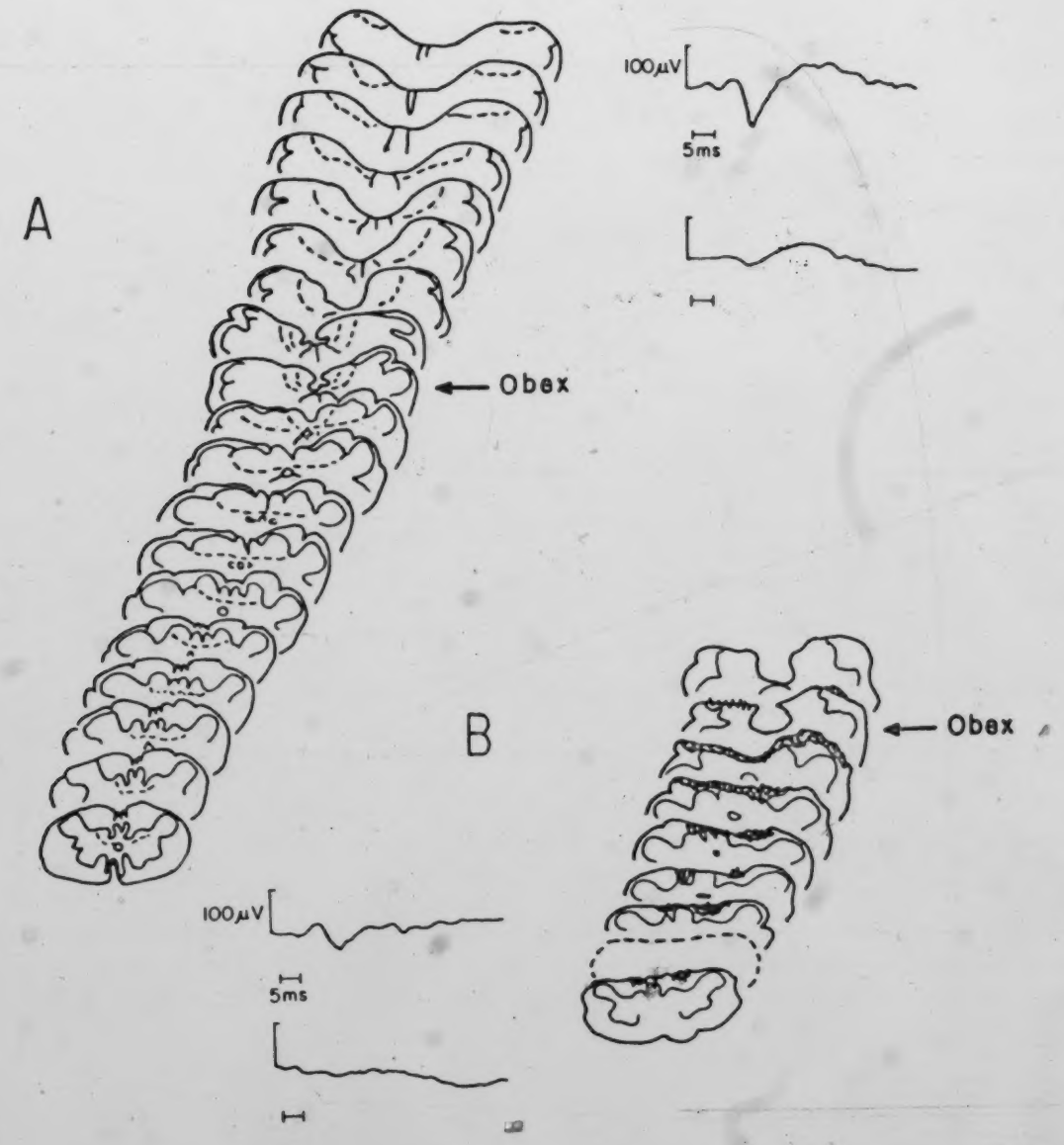

Figure 3. Sham-Operated and Normal Control Animals: See text (sec. 5.1.1.1) for general explanation of Figures 3-7.

A. Sham-Operated Controls, C-116 and C-117: Composite representation. Approximate boundaries of DCN outlined with dashes. No lesion damage shows, thus this diagram represents Normal Control brainstems. Evoked potential record is from C-117. Upper trace represents preoperative activity, lower trace represents postoperative activity.

B. Sham-Operated Control, C-86: Shows superficial damage to fibre tracts overlying DCN.

caudad 3.5 mm. No nuclear material was involved, and since fibre damage was very slight, being limited to the medial aspect of the cuneate tract bilaterally, this animal was retained in the Sham-Op group.

Prior to lesioning, both C-86 and C-117 showed shock-evoked potentials having early negative peaks at about 8.0 msec. following shock onset. Slower positive deflections peak at about 12.0 msec., followed by still slower negative deflections peaking around 28.0 msec. In both animals, amplitudes were somewhat diminished and overall appearance was more variable following lesion surgery. In terminal experiments (not shown), evoked potential activity was similar to that following surgery.

5.1.1.2 RZ-Lesioned Group. Four animals (Fig. 4a. - 4d.) were assigned to the RZ-Lesioned Acquisition Group. These animals displayed damage of nearly equivalent extent and location to the nuclear material of the DCN caudal to the obex. These animals also showed total interruption of fibre tracts which, presumably (see sec. 6.1.2), course rostrally, superficial to the RZ cell bodies.

In C-49 (Fig. 4a.), a patch of gliosis appears superficially 2.5 mm. caudal to the obex. It becomes more extensive rostrally until, at 1.5 mm. caudal to the obex, the fibres overlying the nuclear material are totally transsected. Fibre destruction continues rostrally up to the level of the obex, but becomes narrower in cross-section. Accompanying the fibre destruction, the superficial dorsal areas of nuclear material are absent bilaterally. In addition, deeper material is densely invaded by gliosis.

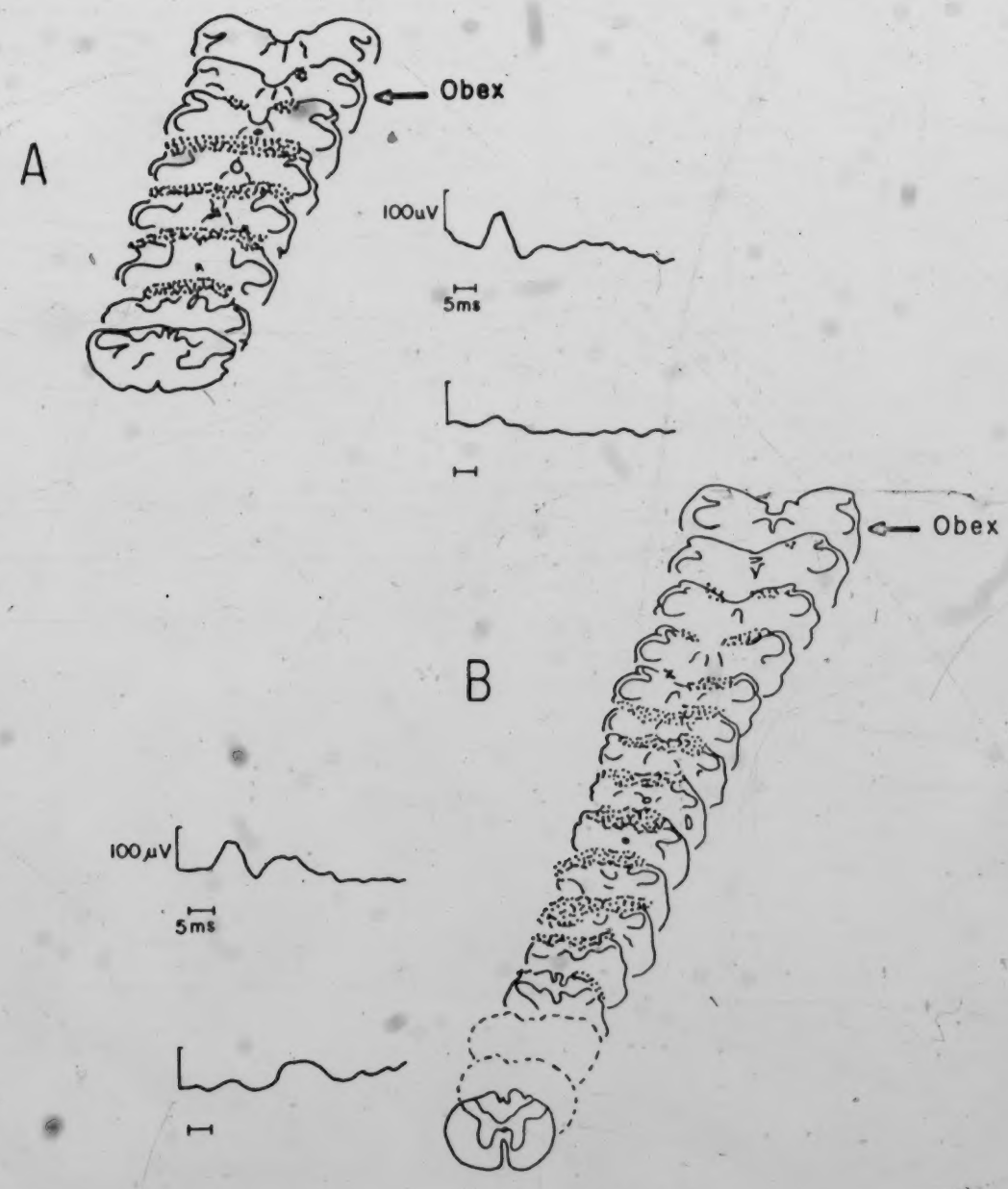

Figure 4. RZ-Lesioned Animals:
A. C-49: In this animal, scar tissue penetrated much deeper than the actual extent of the lesion as shown. Note the destruction of fibre tracts overlying the DCN.
B. C-51: This animal also shows complete fibre tract transection, in addition to DCN lesion.

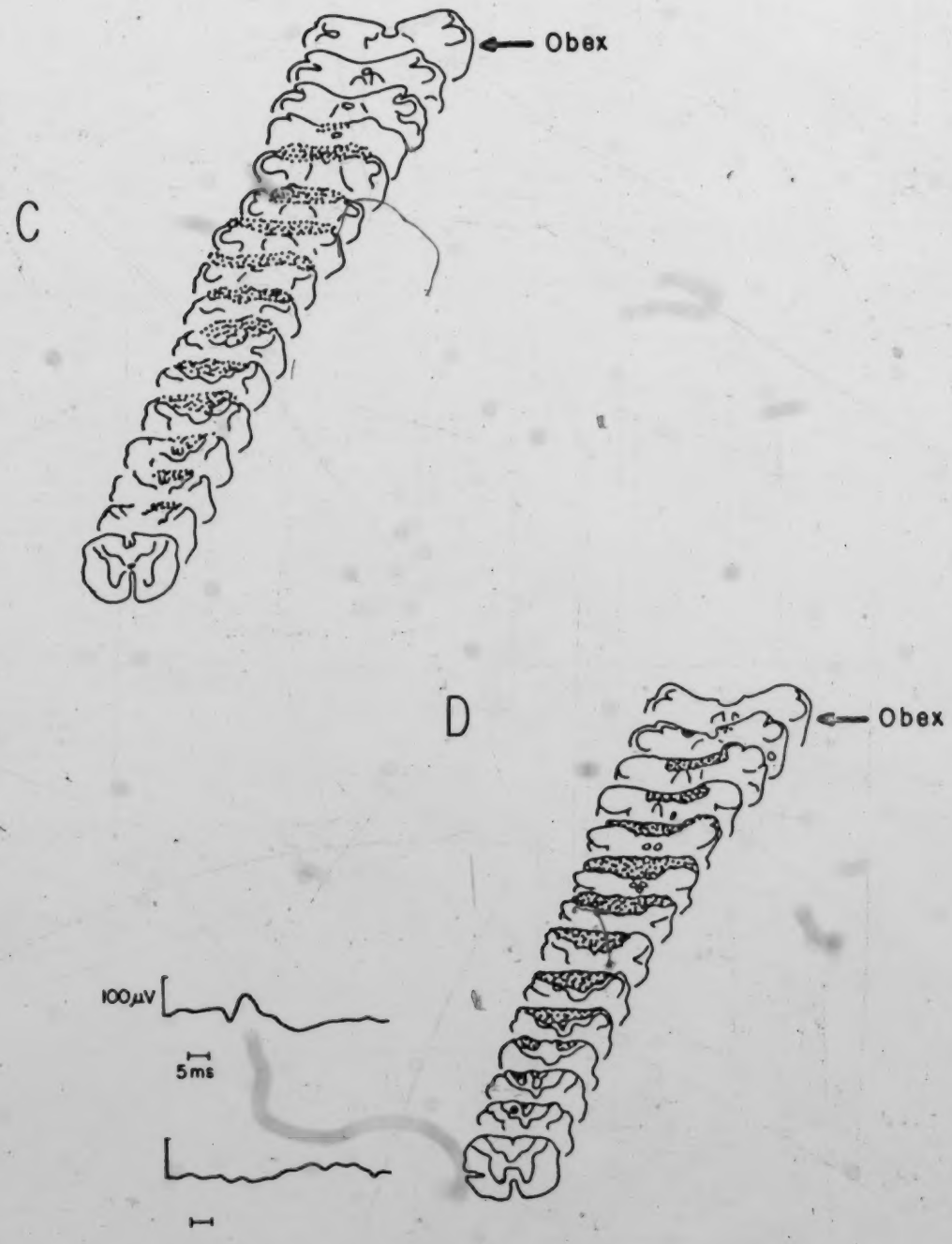

Figure 4. Continued.
C. C-52: No evoked potential data is available on this animal.
D. C-53: Note the common features of the RZ lesions: large involvement of the nuclear material of the DCN and total or near-total transsection of superficial fibres.

In C-51 (Fig. 4b.), superficial glial invastion appears laterally and bilaterally 6.0 mm. caudal of the obex. Half a millimeter rostral, scarred dura mater has invaded the superficial zone of fibre destruction and completely obiterated the nucleus gracilis on both sides. Ablation of the DCN is total from 4.0 mm. to 2.5 mm. caudal of the obex. Extensive damage continues rostrally for a millimeter and a half more. The overlying fibres tracts are completely interrupted.

An almost identical pattern of destruction appears in C-52 (Fig. 4c.). The superficial fibre tracts are entirely severed between 2.5 mm. and 2.0 mm. caudal of the obex. The DCN are totally destroyed from 4.0 mm. up to 2.0 mm. caudal of the obex.

This pattern appears again in C-53 (Fig. 4d.). Damage begins in the left cuneate tract 6.0 mm. caudal of the obex. This widens and becomes total bilateral DCN lesion by 3.5 mm. caudal of the obex. Destruction remain total for a millimeter further rostrally, but narrows and becomes superficial dorsomedial damage at its rostral termination, 0.5 mm. behind the obex. As in the other three animals, the dorsal superficial fibre tracts are completely interrupted.

Evoked potentials recorded preoperatively from three of these four animals displayed roughly the same time and amplitude features as preoperative records taken from the Sham-Op animals. After lesioning, amplitudes were greatly reduced and time features showed increased variability. For C-49 and C-53 the post-lesion records are nearly flat. No recovery of evoked potential activity was obtained in terminal experiments.

5.1.1.3 RTZ-Lesioned Animal. C-125 was the only animal which

possessed a verifiable lesion of the RTZ (Fig. 5). A narrow band of gliosis appears dorsally and superficially about 2.5 mm. caudal of the obex. This gradually widens and deepens until at the level of the obex it totally obscures the gracile nucleus and deeply penetrates the cuneate nucleus. The lesion continues to deepen such that from 0.5 mm. to 2.0 mm. rostral of the obex, both DCN are totally involved bilaterally. The lesion continues, becoming wider but more shallow, up to 3.5 mm. rostral of the obex.

Evoked potentials recorded after lesioning showed a decline in the initial positive deflection. At sacrifice, however, the evoked potential record was flat.

5.1.1.4 Superficial Border-Zone Lesional Group. C-20 and C-35 (Figs. 6a. and 6b., respectively) showed only superficial glial invasion of fibre tracts overlying a cytoarchitectural border zone (BZ) between the RZ and the RTZ. Hence these animals are together termed the Superficial BZ group.

The glial invasion begins about 2.0 mm. caudal of the obex and continues up to the level of the obex. The tissue abnormality possessed by these animals is actually slightly less severe than that of C-86 in the Sham-Op group. This, however, is not clear from the figures.

A slip of the forceps during histological preparation resulted in a staggered bilateral invagination, reaching deep into C-20's brainstem. Thus this abnormality is not part of any lesion.

Post-lesion and terminal evoked potential records in both these animals showed some decline from their preoperative amplitudes. These

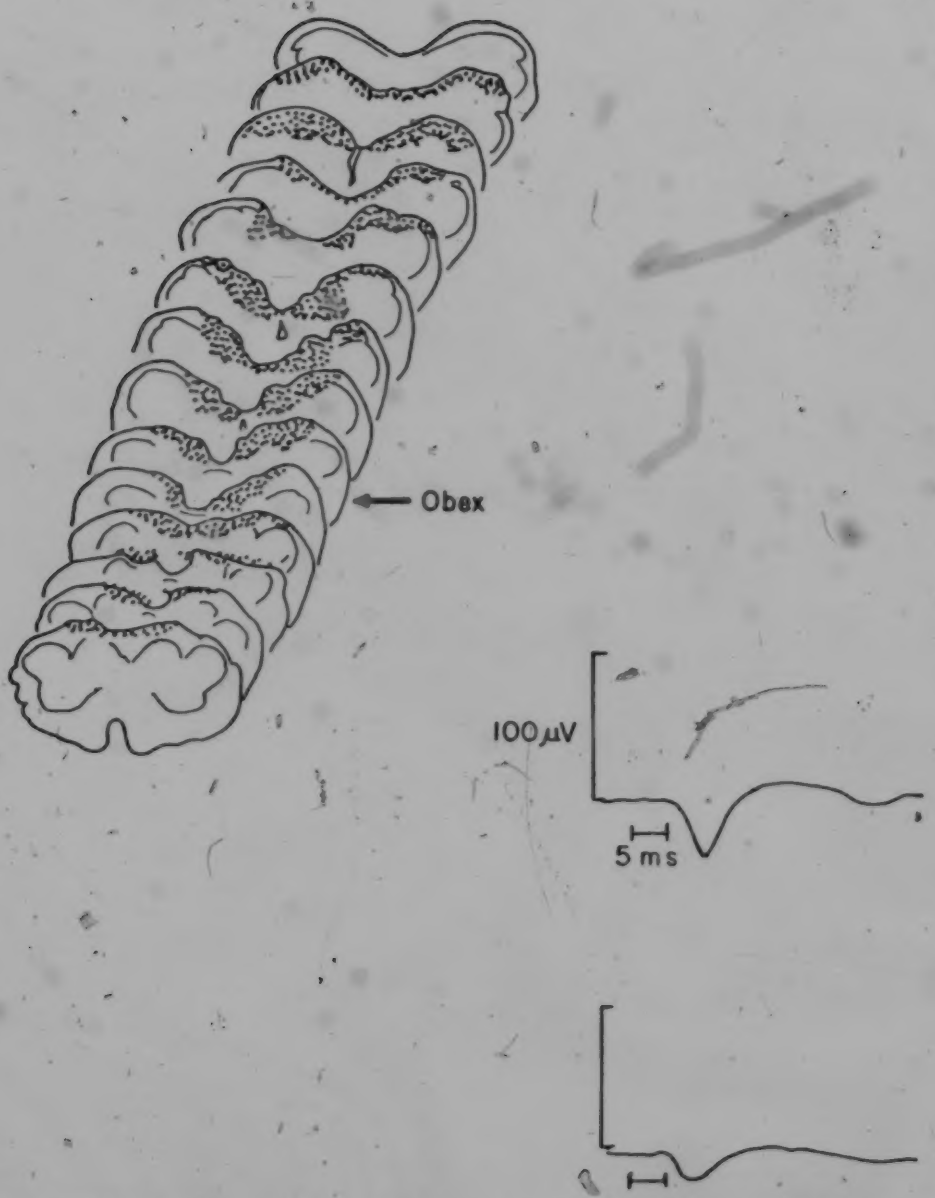

Figure 5. RTZ-Lesioned Animal, C-125: This was the only animal showing significant lesion damage rostral of the obex. This animal showed strong performance deficits in both the walking and reaching tasks, as well as enduring abnormal reflex activity.

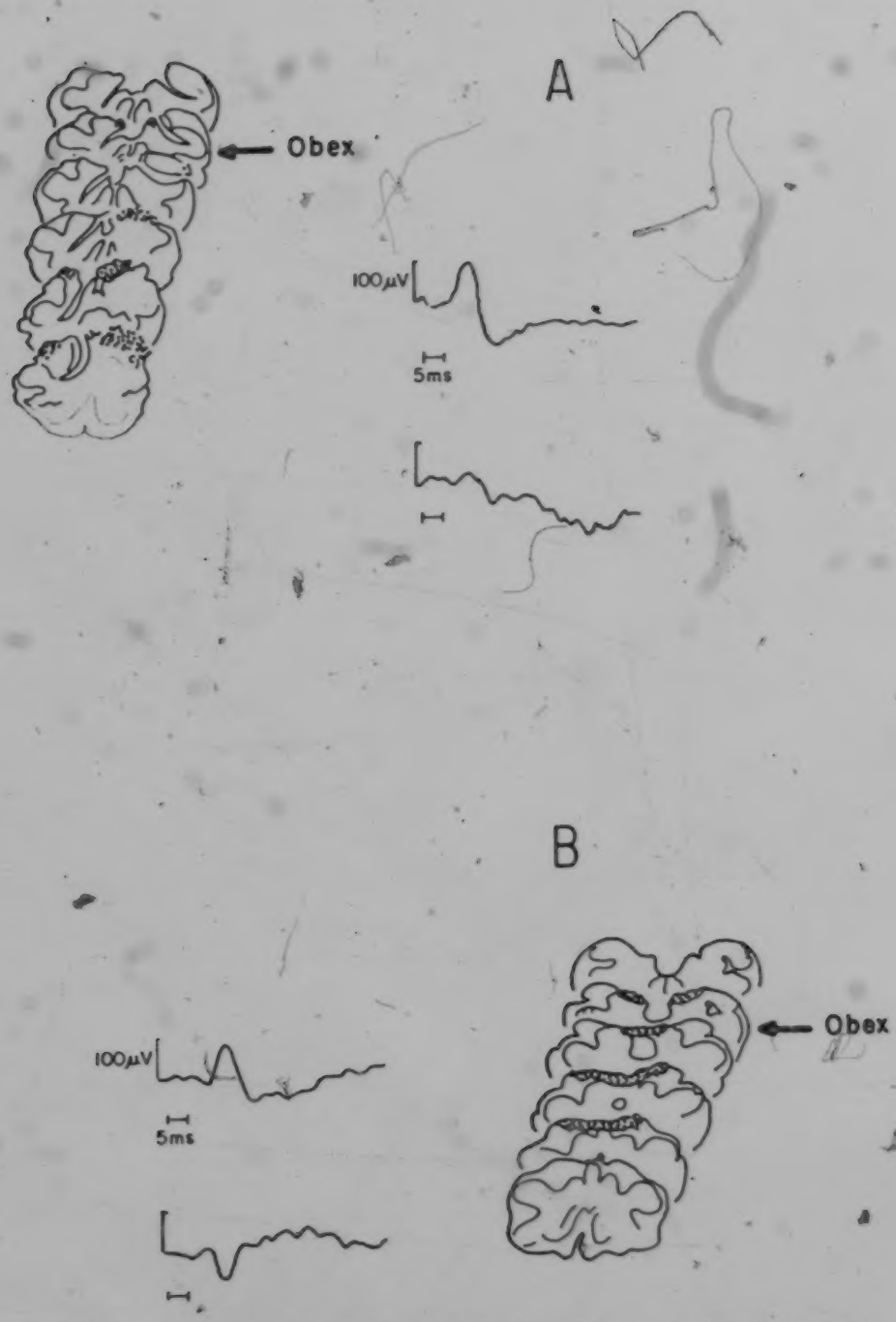

Figure 6. Superficial BZ-Lesioned Animals: These animals showed only superficial involvement of fibre tracts overlying a zone of cytoarchitectural transition between the RZ and RTZ.

A. C-20.
B. C-35.

changes were small, however, compared to those of the RZ-lesioned animals.

5.1.1.5 Border-Zone Lesioned Animal. C-7 survived attempted electrolytic lesioning of the RTZ. Instead of the intended lesion, however, this animal showed bilateral lesioning primarily in the BZ (Fig. 7). Unlike the mild lesions in the Shallow BZ animals, though, the lesions in C-7 are deep, involving large portions of the nucleus cuneatus. On the left side, cuneate involvement begins 2.0 mm. caudal of the obex and continues up to 1.0 mm. rostral of the obex. Similar involvement on the right side begins 3.5 mm. caudal of and ends at the level of the obex. These nuclear lesions are characterized by well-demarcated, globular formations of gliosis.

Another feature distinguishing the BZ lesion from the Shallow BZ lesions is the nearly complete transsection of fibre tracts overlying the RZ 2.5 mm. caudal of the obex. All that continues is a small remnant of cuneate tract fibres on the left side.

Only the initial positive component of the evoked potential could be recorded prior to lesioning. After lesioning this disappeared. Terminal experiments were not possible, as C-7 expired suddenly from unknown causes two months following surgery.

5.1.1.6 Medial Lemniscus Lesions. The ML was successfully lesioned in three animals. Only a single section through the thalamus is represented for each of these three animals (Figs. 8a. - 8c.), as the focus of concern is interruption of a fibre tract in two dimensions, rather than an evaluation of nuclear lesion extent in three dimensions.

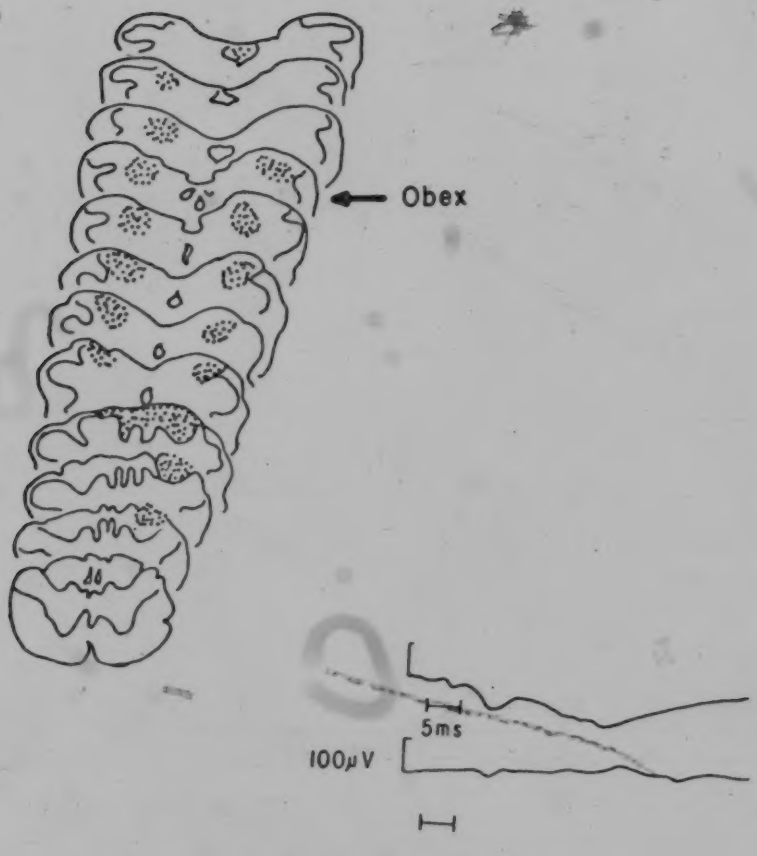

Figure 7. BZ-Lesioned Animal, C-7: Note the staggered appearance of the lesions in the nuclear material. This is due to a slight offset of the lesioning electrodes. This was the only animal which survived attempted electrolitic lesioning of the DCN.

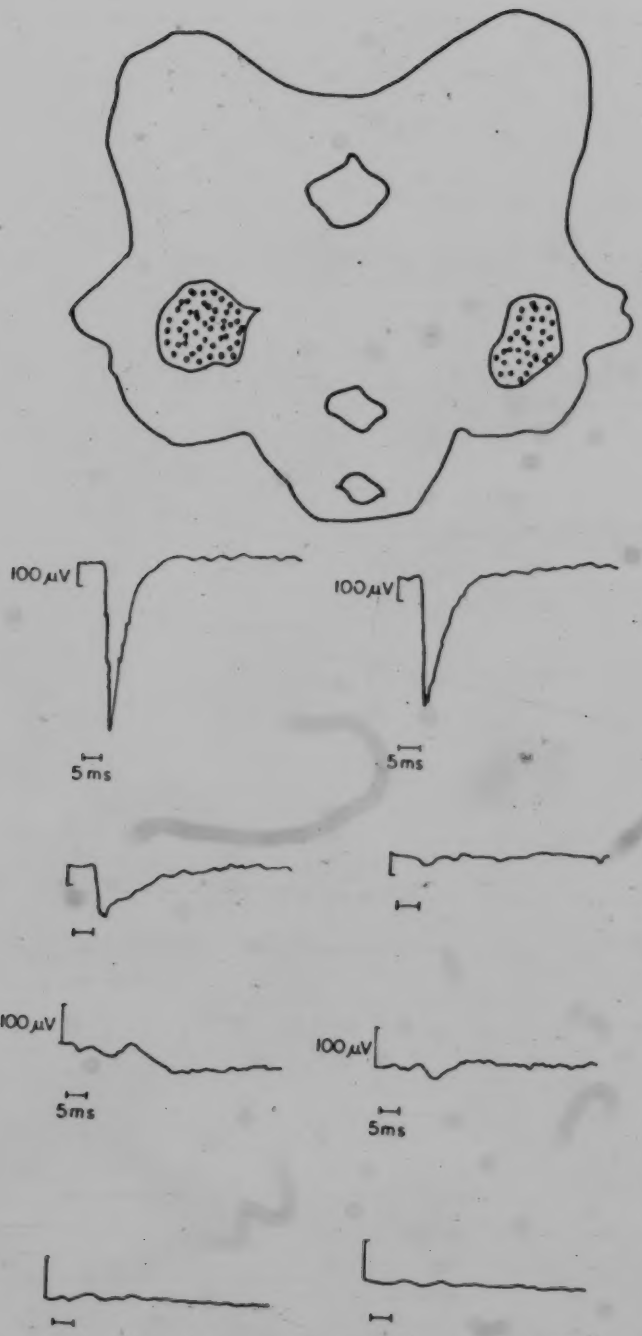

Figure 8A. ML-Lesioned Animal, C-118: Frontal section at A-2.0. In this figure and in Figures 8a., 8b., stippling indicates tissue destruction in region of ML. Pre-lesion ML evoked potentials (top two traces) are much stronger post-lesion ML evoked potentials (second row from top). The same applies to pre-lesion post-sigmoid (third row from top) and post-lesion post-sigmoid (bottom row) evoked potentials.

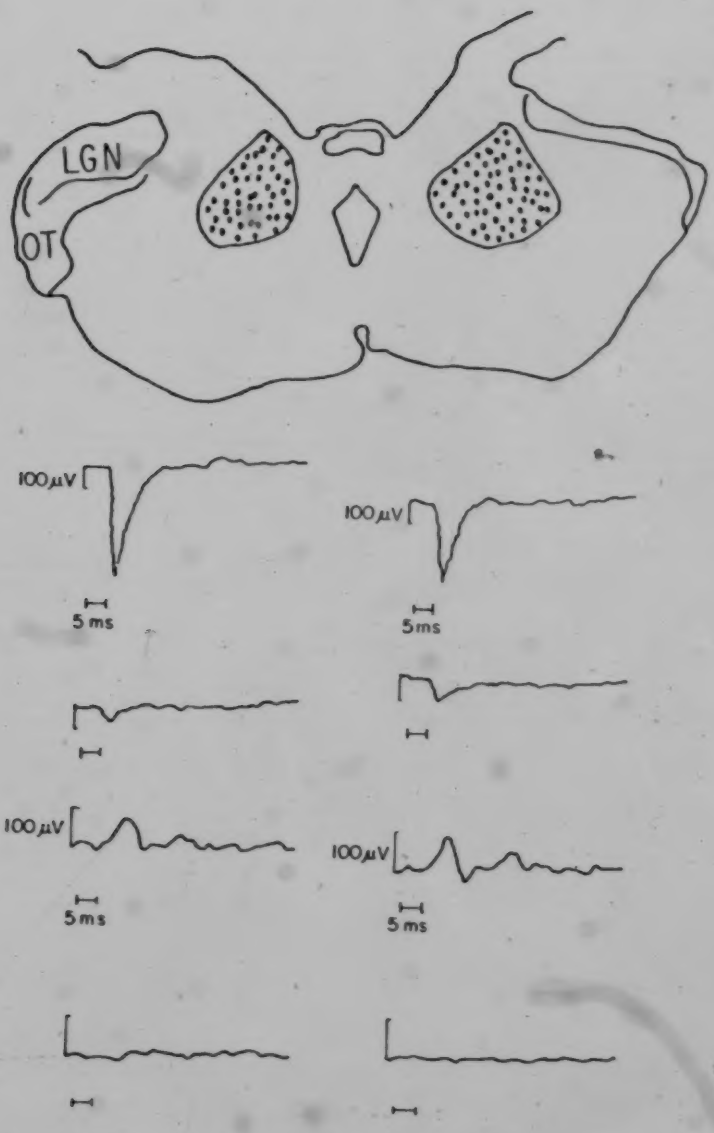

Figure 8B. ML-Lesioned Animal, C-203: Frontal section at A-6.0. Evoked potentials (located in diagram as in Figure 8a.) show changes after lesioning similar to those of C-118 (Figure 8a.). Note absence of LGN on right side, a lesion effect probably accounting for C-203's blindness. Damage to the LGN also appeared on the left side, though it is not diagrammed in this figure. C-118, the other blind ML animal, showed similar damage.

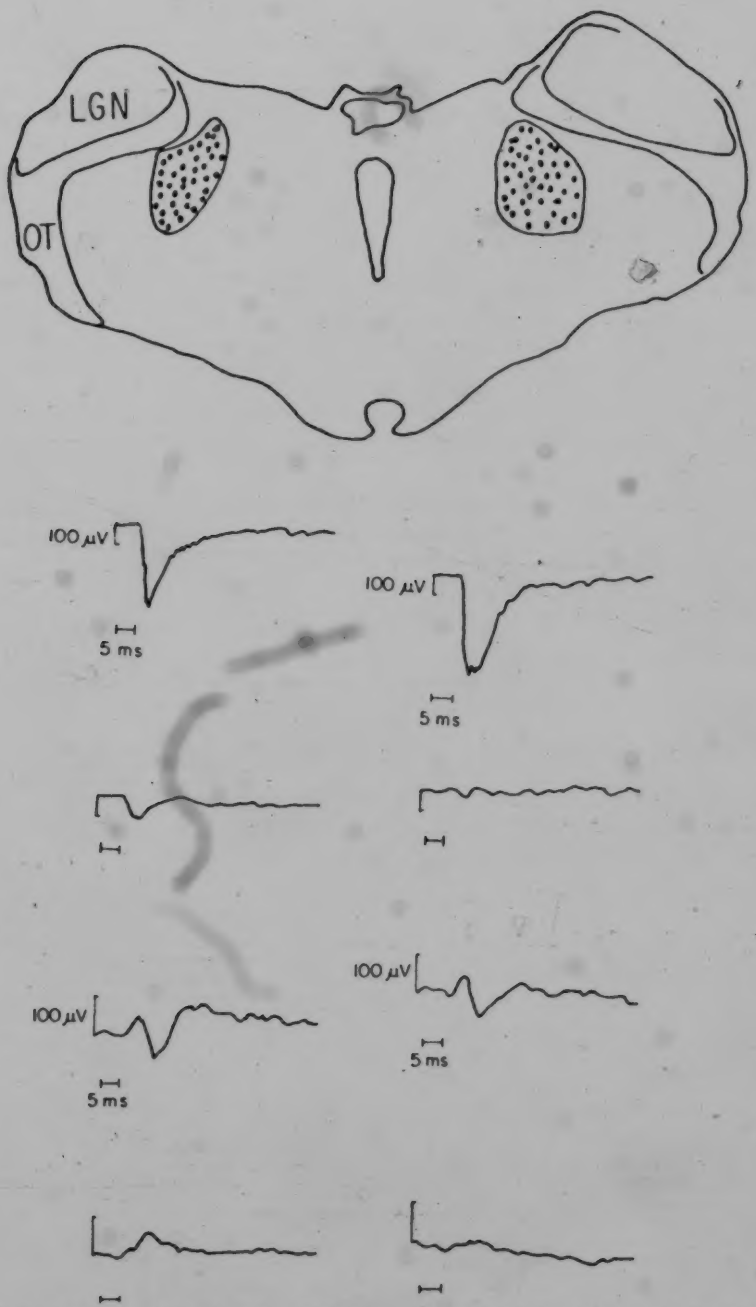

Figure 8C. ML-Lesioned Animal, C-153: Frontal section at A-6.0. This animal shows evoked potential declines following ML lesion, as do the other animals in the ML-Lesion group. Note, however, that the LGN in this animal was left intact. This was the only one of the ML-Lesioned animals that did not show damage to the LGN and which was not blind.

C-118 (Fig. 8a.) shows bilateral ML damage in an area of brainstem located at stereotaxic A-2.0 according to Jasper (1954) and Snider and Neimer (1961). Interruption of the ML was achieved bilaterally in C-203 at A-6.0 (Fig. 8b.). Partial interruption on the left side and more complete interruption on the right side occurs in C-153 (Fig. 8c.).

Lesions in all three animals conform to a teardrop shape, the apex of which is directed along the path of electrode insertion. This is not evident for C-118, as the angle of electrode insertion does not coincide with the plane of section. Lesions measure about 3.0 mm. - 3.5 mm. in diameter. They characteristically consist of a ring of scarred tissue surrounding a central evacuated lumen having a diameter of 1.5 mm. - 2.0 mm.

Before lesioning, all three animals displayed strong evoked potentials bilaterally in the ML. These potentials consisted of a sharp positive deflection ranging in amplitude from 350 microvolts (C-203, right side) to 750 microvolts (C-118, left side). These potentials peaked nearly invariably at 7.5 msec. following stimulus onset. After lesioning, these potentials, recorded slightly rostral of the lesion site, were all markedly reduced. This reduction ranged from at least one-third (C-118, left side) to complete disappearance (C-153, right side).

Characteristic forebrain potentials were recorded from all three animals prior to lesioning. After ML lesioning, only the left side record of 153 showed any remnant of activity. Recovery of evoked potential activity was not detected in terminal experiments.

Certain of the histological findings bear relevance to the apparent blindness observed in C-118 and C-203 (see sec. 5.2.6). In C-118, damage appears bilaterally in the medial aspects of the lateral geniculate body (LGN), the optic tract (OT) and the optic radiation (OR), although this damage is not pictured here. In C-203, the entire LGN on the right side appears to have atrophied. These structures are intact in C-153, the only sighted animal of the three.

5.1.1.7 Summary. Animals were assigned, for purposes of behavioral comparison, to seven groups on the basis of histological and evoked potential data.

There were three retention groups: (1) A group of six unoperated Normal Control animals. (2) A group of two animals with superficial lesions of fibre tracts overlying a cytoarchitectural border-zone (BZ) between the RZ and the RTZ. (3) A "group" of one animal lesioned more extensively in the BZ, with accompanying near-total interruption of superficial fibre tracts.

There were four acquisition groups: (1) A group of three Sham-Op Control animals showing little or no damage in the brainstem. (2) A group of four animals displaying massive RZ damage with accompanying total interruption of overlying fibre tracts. (3) One RTZ-Lesioned animal. (4) A group of three ML-Lesioned animals, two of which were blind.

5.1.2 Verification of RTZ Lesions in Non-Surviving Animals

All animals which did not survive attempted RTZ lesion and for which histological material was available (C-9, C-24, C-38, C-41, C-45, C-46, C-50, C-104) showed at least some damage in the RTZ.

It thus appears that a lesion to this zone can be reliably placed by mechanical or thermocoagulative means.

There exist, however, two major obstacles to the survival of animals with such lesions. First of all, surgical approach to the RTZ requires that much meningeal and ependymal tissue be torn and sheared. This inevitably leads to bleeding, even if done gently. In addition, the act of lesioning itself, whether by thermocoagulative or mechanical means, often induces a flow of blood from brainstem tissue. The source of this hemorrhaging is indefinite and the bleeding difficult to control. Even when it is apparently under control, it may begin again in some animals after lesion surgery is complete and they have been returned to their cages. For example, the fourth ventricles of C-24, C-38, and C-41 were gorged with blood at autopsy. In addition, their brainstems were deformed, presumably from pressure exerted by blood in the ventricle.

The second obstacle to survival is the fact that the medullary cells responsible for the generation of rhythmic breathing movements [redacted]lly coextensive rostro-caudally with the rostral portion of [redacted] (Ransom & Clark, 1959). They lie heavily concentrated between 2.0 mm. - 3.0 mm. below the dorsal surface of the brainstem (Salmoiraghi & Burns, 1960). Thus a successful lesion of the RTZ rostral of the obex which penetrates more deeply than the 1.0 mm. - 1.5 mm. depth of the RTZ itself is likely to have some effect on respiratory function.

Relevant to the above, C-24, C-41, C-45, and C-104 all possessed lesions penetrating deeper than the 1.5 mm. ventral border of the RTZ.

C-45 and C-104 both inspired sharply during the last part of lesioning and did not thereafter exhale. C-45's heart continued to beat for 22 minutes after the beginning of this apneustic spasm, until artificial respiration was no longer sufficient to maintain life. C-46 showed a similar apneustic spasm, even though histology showed that the lesion in this animal was relatively shallow.

Remedies to problems created by these results will be taken up in the Discussion (see sec. 6.2.2).

5.2 Surgical Recovery and General Behavioral Observations

5.2.1 Sham-Operated Controls

C-86 registered the most rapid postoperative recovery of the Sham-Op animals. This animal was conscious 20 hours after surgery and soon sat up and responded in an alert manner. However, it sat in a "kittenish" posture--between its legs rather than on top of them. Tactual placing responses were either weak or absent. Two days after surgery a wobbly stance was noted. The stance was also wide-based, but not to the degree noted in cerebellar animals by other workers (Bourassa, 1977). By five days postoperatively both stance and reflex abnormalities had disappeared and the animal walked in an apparently normal fashion.

The two Sham-Op animals showing no brainstem lesioning initially recovered somewhat more slowly. C-116 was not fully active and alert until 48 hours. C-117 did not recover consciousness until 66 hours, but was alert and active by 72 hours. Both animals displayed signs on the third day similar to those of C-86. But, as in C-86, these disappeared by the fifth day.

5.2.2 RZ-Lesioned Group

The RZ-Lesioned animals were more conspicuously and less transiently affected than the Sham-Ops.

C-53, although awake and responsive 24 hours after surgery, was not able to sit or stand up until the sixth day. In the interim, the animal got about the cage by creeping. During this same period, withdrawal reflexes could be elicited only by very strong pinching. Moreover, they were slow, unlike the rapid and sensitive withdrawal reflexes shown by the Sham-Op animals as soon as they had regained consciousness. On the day that the animal stood for the first time, withdrawal reflexes became brisk. Sitting, standing, and walking were characterized by kittenish splaying of the limbs. Gait was wobbly and the animal often seemed on the verge of tipping over. The animal's walking displayed a curious "skating" or "shuffling" feature. The footpads would slide along the floor a bit after they had made contact with the floor. This feature appeared to replace the normal "yield" which characterizes this particular part of the feline step (Lundberg, 1969). This abnormality persisted throughout the entire survival period of the animal. Tactile placing reflexes were absent from all four limbs during the first six days. They gradually recovered afterwards, except in the right forelimb, in which they never recovered.

C-49 showed the most dramatic debilitation in the RZ-Lesioned group. Periods of extensor tonus alternated with periods of flexor tonus during the first three postoperative days. Although C-49, like C-53, was alert, responsive, and able to creep about the cage by the

third day, its limb movements seemed less finely directed and more "ballistic" in nature. The other RZ animals showed a strong righting reflex as soon as they had regained consciousness. But this reflex did not recover in C-49 until the third postoperative day. Even then it was slow, as the animal took at least five seconds to right itself after being placed on its back. Righting assumed its characteristic rapidity by the end of the first week. If the animal was placed in unnatural positions during the first week, it tended to stay in them. This was similar to the "catatonic" feature of DC lesion deficit described by others (sec. 2.4.2). The animal did not attempt to stand until the ninth day and did not succeed in doing so until the twelfth day. Thereafter, and throughout the survival time of the animal, walking was greatly disturbed, in a manner nearly identical to that described for C-53. No tactile placing responses were observed until the sixth day. Their presence during the remaining survival period seemed to depend somewhat on the concurrent flexion and extension of limbs not being tested.

C-51 and C-52 were somewhat less conspiciously affected than the other RZ animals. C-51's rate of recovery was similar to that of C-86 of the Sham-Op animals. No reflex abnormalities were observed save for a brief period of sluggishness after the animal had regained consciousness at about 30 hours. This animal began to walk in a normal fashion after about four days of kittenish stance and gait. C-52's recovery was nearly identical, except that the stance and gait abnormalities took a week to disappear.

5.2.3 RTZ-Lesioned Animal

The RTZ animal (C-125) regained consciousness within 24 hours of surgery. It was alert and playful, but did not succeed in standing until the seventh day. The animal also started walking on the same day, but could take no more than two steps without its forelimbs collapsing. Gait was characterized by poor synchronization of the forelimbs and hindlimbs. Stance was wide and kittenish in the forelimbs, but not in the hindlimbs. Over the next five days the forelimb stance became more normal and limb synchronization improved. The hindlimbs, however, developed a curious stiffness, seen in no other animal in this study. They seemingly swung from the hip without marked changes in relative angles of the knee and ankle joints. As in the two most seriously affected RZ animals, yield was lacking, but replaced in this case with stiffness rather than flaccidity. This hindlimb stiffness perservered throughout the survival period.

Placing, both visual and tactile, was difficult to elicit during the first four days, although support reflexes seemed intact from the start. Placing recovered within the first ten days with the exception of the left hindlimb, in which it never recovered. Another feature unique in this study was C-125's poor control over claw retraction and protraction during the first nine days. This recovered fully, except, again, in the left hindlimb.

5.2.4 Superficial Border-Zone Group

C-20 and C-35 showed the most rapid surgical recoveries. Both these animals were alert and active 18 hours following surgery. Also

at that time, they sat, stood, walked, ran, and jumped as they had done prior to surgery. Reflex testing revealed no abnormalities. These animals were to all appearances without deficit.

5.2.5 Border-Zone Lesioned Animal

The animal with comparatively deep lesions in the BZ (C-7) displayed a severe walking deficit, which remained while the animal survived.

C-7 had regained consciousness and was attempting to stand 36 hours after surgery. Its attempts were marked by placing on the dorsum of the forepaw rather than the pad, a feature of deficit shown by no other animal in the present work. The animal succeeded in standing and walking by the end of the third day, but displayed all the walking deficit features described for C-49 and C-53 (sec. 5.2.2) except shuffling. Splaying of the toes in all four limbs was pronounced, especially during attempts to walk. The animal, when walking on the floor, always tended to "drift" toward the left in a comical "drunken" fashion.

Placing, righting, and withdrawal reflexes were difficult to assess, as C-7 habitually bit and scratched the experimenter whenever handled.

5.2.6 Medial Lemniscus Lesioned Group

All three of the ML-Lesioned animals showed severely disrupted reflex activity during the first postoperative week. Strong extensor tonus alternated with strong flexor tonus for about the first four days.

Also during the first four days, C-118 and C-153 often displayed

a "pedaling" motion of the forepaws if touched anywhere on the body. This pedaling resembled in some respects the spontaneous locomotor activity seen in certain decorticate preparations (Grillner, 1975; Wetzel, 1976). Placing, when it could be tested during periods of relatively normal muscular tonus, was generally weak or absent. It recovered abruptly in all three animals before the end of the first week. This is in contrast to animals with DCN lesions, in which it recovered gradually.

On the same day placing reflexes recovered, animals stood for the first time. C-118 showed kittenish sitting, standing, and walking until the twelfth day. No walking or reflex abnormalities were observed in C-153 or C-203 after nine days.

Animals C-118 and C-203 were apparently blind according to the rough clinical measures used. Both animals readily oriented to sounds made in the colony room but failed to orient to objects or bright lights moved through the visual field. These visual tests elicited enthusiastic orienting from C-153 and normal animals. C-118 intermittently responded with pupillary constriction to a rapidly approaching fingertip, yet failed to orient toward it. C-203 showed no pupillary responses. After tactile placing had recovered in these animals, contact would always elicit placing. However, surfaces of very high contrast were required to elicit visual placing of limbs. This apparent blindness endured up to the time of sacrifice.

5.2.7 Summary

Most animals with large lesions (sec. 5.1.1) showed, at most, transient disturbances in reflexes and locomotor activity which

disappeared within a week to ten days. Exceptions were the two most seriously affected RZ animals, the RTZ animal, and the BZ animal. In these, a walking deficit characterized in general by a wide, kittenish stance endured throughout the postoperative survival period. The two most seriously affected of the RZ animals tended to "shuffle." Stiff hindlimbs, which tended to swing from the hip rather than display articulated stepping, were unique to the RTZ animal. Placing reflex abnormalities also endured in these four exceptional animals.

In addition to transient walking and reflex deficits, two of the three animals showing ML lesions were blind. The Sham-Operated animals showed the most transient deficits of all. The two animals with superficial lesioning over the BZ showed no abnormalities whatever.

5.3 Walking Task Results

5.3.1 Judgement Reliability

Using video-taped samples of walking behavior for each animal, judgement reliabilities (Table 2) were computed for three cases: (1) Rate-Rerate Reliability: The original observer's first observations were compared to his second observations. (2) Independent Inter-Rater Reliability: The original observer's first observations were compared to the observations of a second observer, briefed in judgement criteria. (3) Non-Independent Inter-Rater Reliability: The original observer's second observations were compared to the second observer's observations, made while the original observer coacted the second observer. Reliabilities were computed for each type of error. Significance leads for each coefficient are given (Hays, 1961)

Note that, except for paw placement errors, the highest

Table 2

Walking Task: Judgement Reliabilities

	Rate-Rerate	Independent Inter-Rater	Non-Independent Inter-Rater
Errorless Trials	.90*	.91*	.98*
Total Errors	.80*	.81*	.94*
Paw Slips	.76*	.53+	.97*
Pivoting Errors	.83*	.81*	.93*
Paw Placement	.83*	.65+	.77*
Falls	.77*	.52+	.87*

*p. alpha < .001

+p. alpha < .05

reliabilities obtain for the non-independent case. For the Errorless Trials and Total Errors judgements, the independent inter-rater case reliabilities are somewhat lower, though still high and significant. Thus judgement criteria were transferred from one observer to the next (non-independent case) and were used by the second observer in a fashion similar to that used by the first observer originally (independent case).

Coefficients for the Errorless Trials and Total Errors reliabilities are almost identical between the rate-rerate and independent inter-rater cases. This suggests that judgement criteria are generally stable over time and that the same observer or a confederate can apply them repeatedly with nearly equivalent results.

The reliabilities also reflect the relative difficulties of the judgements involved. Reliabilities are higher for errorless trials than for total errors. This indicates that agreement that an error had occurred was better than agreement on how many errors had occurred in a given trial. The slightly reduced level of agreement in the later case resulted primarily from separate errors being scored as single errors, and vice versa, in a continuous sequence of movements.

Coefficients for individual types of errors are generally lower yet. This reflects the frequent disagreement as to the specific types of error being committed. For instance, the first observer tended to rate certain borderline cases as Paw Slips, while the second observer tended to rate them as Paw Placement Errors.

From this analysis of judgement criteria, it must be kept in mind that even though separate errors are compared in the following

section, these comparisons are mitigated somewhat by their relatively unreliable measurement. Errorless trials and total errors are, as measurements, somewhat more reliable indicators of performance.

5.3.2 Walking Task Behavior--Comparisons and Analysis

Figures 9 and 10 display the cumulative ten-day individual and group performances of animals according to the Errorless Trial, Total Errors, and error subclass measurements.

The animals with verified lesions of the DCN (C-7, C-49, C-51, C-52, C-53, C-125; sec. 5.1.1) performed more poorly than normal animals, both by the Errorless Trial and Total Error measurements. In general, the severety of deficit as evaluated by these measures corresponds well with the severity of deficit as evaluated by neurologic testing (sec. 5.2).

Regardless of lesion group, those animals which displayed relatively enduring impairments of walking and normal reflex activity (C-49, C-53, C-7, C-125) also made the most errors and scored the fewest errorless trials. These animals walked the beam only with great difficulty on the first postoperative testing day. C-7 (BZ lesion) appeared unable to progress except by spasmodic leaps during the first day. This was in marked contrast to this animals preoperative performance, which was better than that of any of the other Normal Controls by both measures used (Figs. 10, 11; note that C-7 appears twice in these figures, preoperatively as an NC animal and postoperatively as the BZ animal. Note that the same applies to C-20 and C-35, which appear as the "SBZ" group postoperatively). During the first few days of postoperative testing,

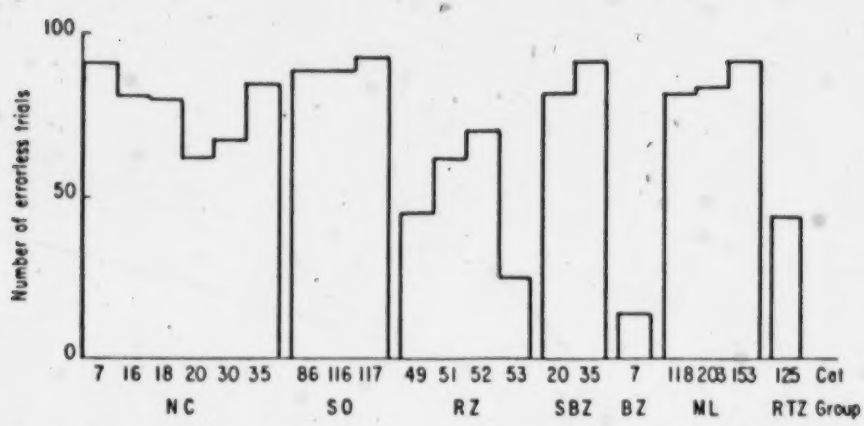

Figure 9. Walking Task, Errorless Trials Measurement: NC=Normal Control Animals. SO=Sham-Operated Control Animals. RZ= Relay Zone Lesioned Animals. SBZ=Superficial Border Zone Lesioned Animals. BZ=Border Zone Lesioned Animal. ML= Medial Lemniscus Lesioned Animals. RTZ=Reticular Zone Lesioned Animal. Note that C-7, C-20, and C-35 each appear twice, once in the NC group and once each in one of the lesion groups.

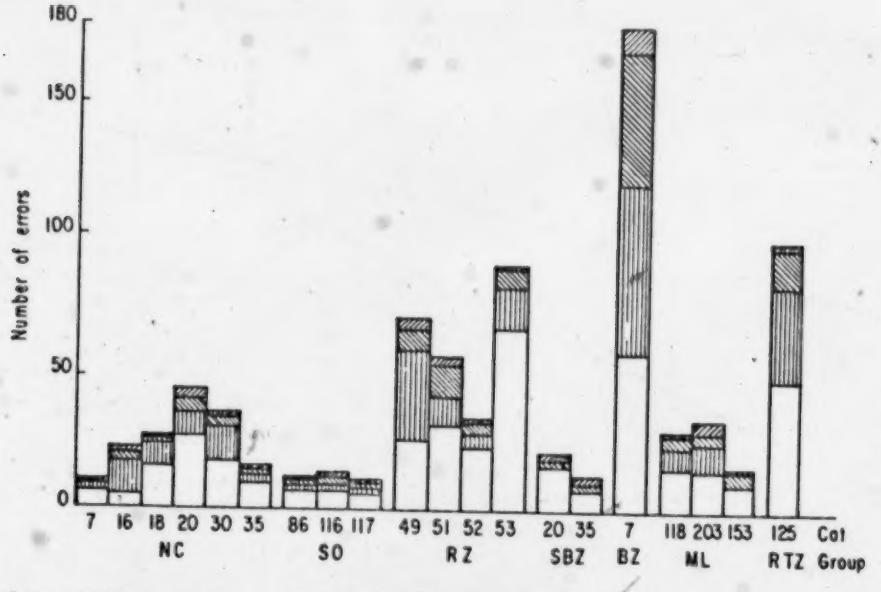

Figure 10. Walking Task, Error Measurement: Animals and groups as in Figure 9. Bar Sinister diagonals=Falls. Bar Dexter diagonals=Paw Placement Errors. Vertical hatches= Pivoting Errors. White=Paw Slips. Full height of each vertical bar represents Total Errors for that animal.

C-7, rather than walking along the top of the beam as it had done preoperatively, tended to grip its sides. This ensured lateral stability, which was lacking in this animal even in normal walking situations (sec. 5.2.5). C-49 and C-53 (RZ group) progressed in a low crouch, unlike any of the Normal Control or Sham-Op animals, which progressed in a normal feline walk. Progression was not characterized by such severe early disability in C-51 and C-52 (RZ group), or C-125 (RTZ lesion), although these animals showed, in general, more frequent errors and fewer errorless trials than control animals.

The nonparametric Mann-Whitney U test (Siegel, 1956) was used, where numbers allowed, for statistical comparisons of group performances. Significant differences between the Sham-Op and RZ-Lesioned animals were obtained in both the Errorless Trials (Table 3a.) and Total Errors (Table 3b.) measures.

The ML-Lesioned animals also showed a significant deficit according to Total Errors (Table 3b.), but not according to Errorless Trials (Table 3a.). Note (Figs. 9, 10) that the performance of the ML-Lesioned animals is only slightly depressed compared to that of the lesioned animals. The performance of the RZ-Lesioned animals is found to be signiiicantly poorer than ML-Lesion performance on both the overall measures (Tables 3a., 3b.). Recall that two of the three ML-Lesioned animals were, in addition, blind (sec. 5.2.6). Yet, the poorest ML-Lesion performance was still better than the best DCN-Lesion performance. None of the ML animals showed any of the early difficulties displayed by some of the DCN animals. In addition, their errors did not tend to compound (e.g., the superimposition of a Paw

Table 3

Walking Task Comparisons

3a. Errorless Trials

Groups	N_1	N_2	U	
NC-SO	6	3	2	$p \leq .05$
NC-SBZ	6	2	3	NS
SO-RZ	3	4	0	$p \leq .05$
SO-MLL	3	3	2	NS
RZ-MLL	4	3	0	$p \leq .05$

3b. Total Errors

NC-SO	6	3	6	NS
NC-SBZ	6	2	3	NS
SO-RZ	3	4	0	$p \leq .05$
SO-MLL	3	3	0	$p \leq .05$
RZ-MLL	4	3	0	$p \leq .05$

3c. Paw Slips

NC-SO	6	3	4	NS
NC-SBZ	6	2	2	NS
SO-RZ	3	4	0	$p \leq .05$
SO-MLL	3	3	0	$p \leq .05$
RZ-MLL	4	3	0	$p \leq .05$

3d. Pivoting Errors

NC-SO	6	3	2	NS
NC-SBZ	6	2	0	NS
SO-RZ	3	4	0	$p \leq .05$
SO-MLL	3	3	0	$p \leq .05$
RZ-MLL	4	3	2.5	NS

Table 3

Walking Task Comparisons (Continued)

3e. Paw Placement Errors

Groups	N_1	N_2	U	
NC-SO	6	3	5	NS
NC-SBZ	6	2	3	NS
SO-RZ	3	4	0	$p \leq .05$
SO-MLL	3	3	3	NS
RZ-MLL	4	3	0	$p \leq .05$

3f. Falls

NC-SO	6	3	8	NS
NC-SBZ	6	2	1	NS
SO-RZ	3	4	5	NS
SO-MLL	3	3	3.5	NS
RZ-MLL	4	3	5	NS

3g. Improvement: Same Group, First to Tenth Day, Errorless Trials

NC	6	6	17	NS
SO	3	3	4	NS
RZ	4	4	0	$p \leq .05$
MLL	3	3	3	NS

3h. Improvement: Same Group, First to Tenth Day, Total Errors

NC	6	6	14	NS
SO	3	3	3	NS
RZ	4	4	0	$p \leq .05$
MLL	3	3	4	NS

Placement Error and a Fall onto a Pivoting Error), as did those of the DCN-Lesioned animals. The early poor performance of the DCN animals improved. However, such improvement did not occur in the performance of other groups, which started off at and maintained relatively high levels of performance. Thus, when the first and tenth testing days are compared (numbers allowing), only the RZ-Lesioned animals show significantly improved performance, and this in both scoring categories (Tables 3g., 3h.).

Certain observations regarding error sub-categories are reflected in the statistical comparisons. For instance, animals with lesions often pivoted in a series of halting approximations. This was unlike the smooth 180-degree, hindlimb-based turn shown by unlesioned animals. Thus the ML and the RZ animals differ significantly from the Sham-Ops in Pivoting Errors measure (Table 3d.). The ML animals slipped significantly more often than the Sham-Ops, but significantly less often than the RZ animals (Table 3c.). The ML animals differed significantly from the RZ animals in Paw Placement Errors, but not from the Sham-Ops, as did the RZ animals (Table 3e.). There were no significant between-group differences in Falls.

Recall (sec. 4.2.1.1) that all animals tested preoperatively walked a narrow beam. Recall also that several of the lesioned animals were unable to walk the narrow beam and were thus trained and tested on a wider beam. In addition, the two animals which received minimal fibre tract damage over the BZ (sec. 5.1.1.4) refused to walk the narrow beam postoperatively, even though they were trained on it preoperatively. It thus became necessary to assess whether or

not the relatively easier postoperative task, after preoperative training on a more difficult task, tended, in itself, to improve postoperative scores. Thus the Sham-Operated animals, which were tested postoperatively on the wide bar, were compared to the Normal Control animals, which were tested preoperatively on the narrow bar. The hypothesis was that testing on the wide bar should result in significantly fewer errors and significantly more errorless trials in non-lesioned animals than testing on the narrow bar. The only significant difference appeared in the Errorless Trials Comparison (Table 3a.).

With only one scoring category affected by the task variable, it was thus considered meaningful to compare the Normal Control animals to the Shallow Border Zone animals. In these comparisons (Tables 3a.-3f.), no significant retention differences were obtained in any of the scoring categories. Note, however, that the postoperative performances of these animals (C-20, C-35) are somewhat improved over preoperative performances (Figs. 9, 10).

To summarize: Animals with DCN lesions show deficits in the beam-walking task which tend to improve over the postoperative testing period. Especially severe deficits correspond to lesioning of the BZ or RTZ. Animals with ML lesions show detectable deficits, though they are significantly milder than those which appear in RZ-Lesioned animals. This is in spite of blindness in two of the three ML animals.

5.4 Reaching Task Results

Figure 11 displays the number of trials animals required to reach training criterion under conditions already described (sec. 4.2.2.2).

Figures 12, 13, and 14 present cumulative scores for the ten-day post-criterion performance measures: (1) Efficiency (proportion of releases/attempts, Fig. 12). (2) Accuracy (number of hits on holder without releasing bait, Fig. 13). (3) Tracking (frequency of localizations in greater than or equal to three seconds, Fig. 14). Note that high scores in Efficiency and low scores in Accuracy and Tracking indicate the better performance. Some animals tested in the walking task were not tested in the reaching task, or parts of it, because of training difficulties (C-7, C-16, C-18, C-49) or blindness (C-118, C-203).

In all four scoring categories individual variability in performance tends to override differences among groups. C-52 (RZ group), C-153 (ML animal), and C-125 (RTZ animal) which show relatively poor performance in the Training, Efficiency, and Accuracy measurements. Certain considerations, however, regarding motivation and reaching strategy, render interpretation of the scores of these animals difficult (sec. 6.1.3).

The only significant difference which emerged in statistical testing (Tables 4a.-4d.) was that non-lesioned animals (Sham-Ops and Normal Controls combined, justified and done on the basis of no significant differences between these groups) took fewer trials to achieve training criterion than RZ-Lesioned animals (Table 4a.).

5.5 Summary of Results

A group of four animals with lesions of the RZ and total transection of overlying fibre tracts displayed a strong walking deficit.

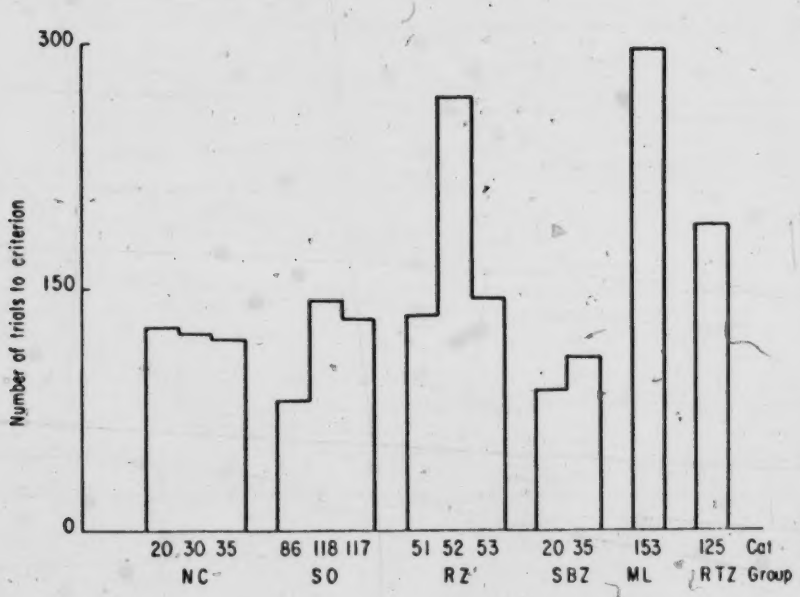

Figure 11. Reaching Task, Training Measure: Each vertical bar represents number of trials animal required to meet training criterion level of performance. Legend for animals and groups as in Figure 9. Note that some animals present in Walking Task are absent from Reaching Task. See text for explanation.

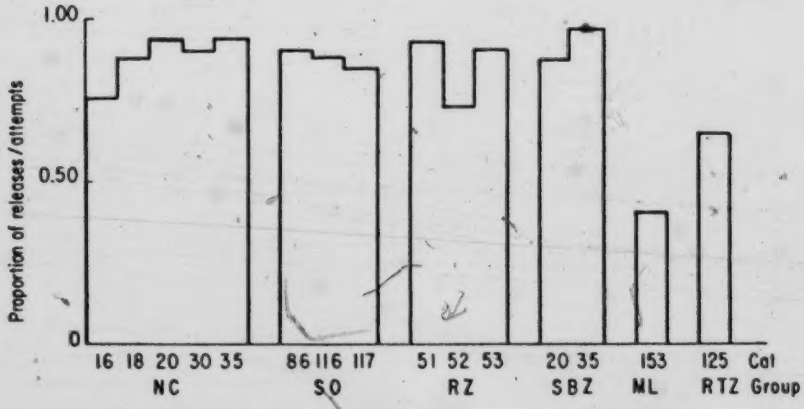

Figure 12. Reaching Task, Efficiency Measure: Each vertical bar represents the proportion of successful releases of bait over the total number of attempts to reach bait. Legend for groups and animals as in Figure 9.

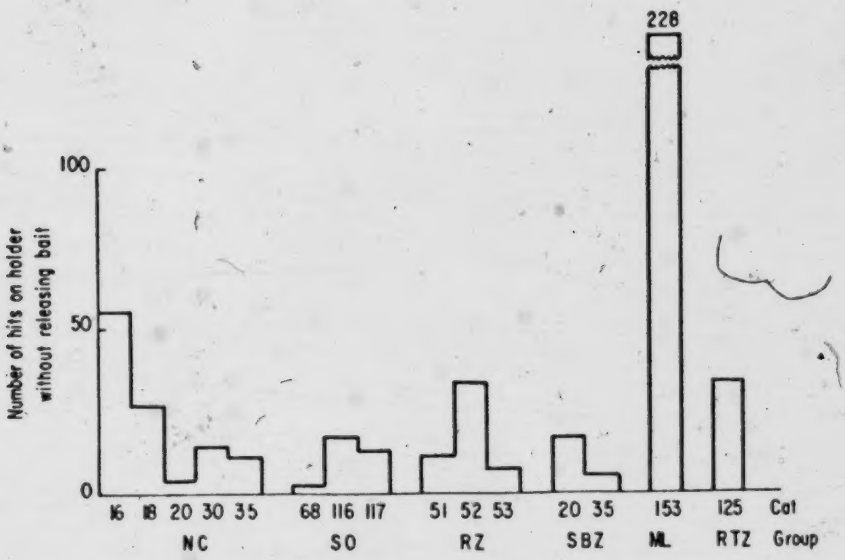

Figure 13. Reaching Task, Accuracy Measure: Each vertical bar represents the number of trials in which animals struck the bait holder with insufficient accuracy to release bait. Legend for groups and animals as in Figure 9.

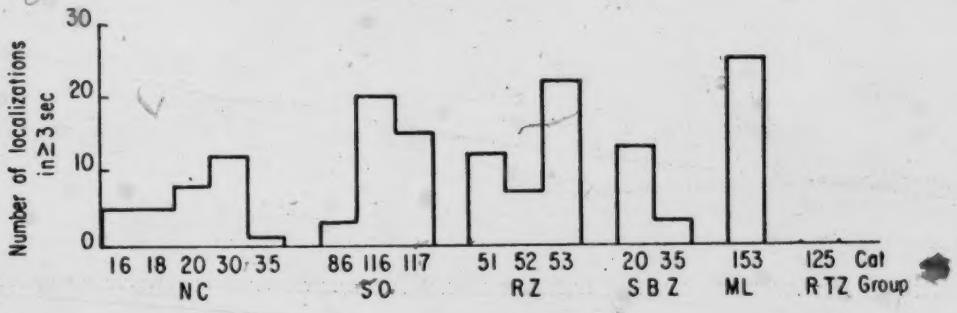

Figure 14. Reaching Task, Tracking Measure: Each vertical bar represents the number of times an animal failed to find the bait on the floor within three seconds of having released it from the bait holder. Legend for groups and animals as in Figure 9.

Table 4

Reaching Task Comparisons

4a. Training: Trials to Criterion

Groups	N_1	N_2	U	
NC-SO	3	3	4	(NS)
NC + SO - RZ	6	3	2	$p < .05$
SO-RZ	3	3	2	(NS)

4b. Performance: Efficiency

NC-SO	5	3	6	(NS)
NC + SO - RZ	8	3	12	(NS)
SO-RZ	3	3	3	(NS)
NC-SBZ	3	2	4	(NS)

4c. Performance: Accuracy

NC-SO	5	3	5	(NS)
NC + SO - RZ	8	3	11.5	(NS)
SO-RZ	3	3	4	(NS)
NC-SBZ	5	2	3	(NS)

4d. Performance: Tracking

NC-SO	5	3	4	(NS)
NC + SO - RZ	3	8	6	(NS)
SO-RZ	3	3	3	(NS)
NC-SBZ	5	2	4	(NS)

One animal with a verified RTZ lesion showed a comparatively stronger walking deficit, although a statistical test was not possible. Neither was it possible in the case of one animal lesioned in a cytoarchitectural Border Zone (BZ) between the RZ and the RTZ. This animal, which showed the best preoperative walking performance among the Normal Control animals, showed the worst postoperative walking performance in the study.

These walking deficits in DCN-Lesioned animals tended to improve over the postoperative testing period. This was in spite of enduring walking and reflex abnormalities in a majority of these animals, observed outside the testing situation.

A mild walking deficit was registered by the ML-Lesioned animals. This deficit was significantly less severe than the DCN-Lesion deficits, in spite of the fact that two of the three ML-Lesioned animals were blind. The performance of these animals, however, did not improve significantly over the postoperative testing period. No enduring walking or reflex deficits were detected in these animals by neurological observation.

Two animals with insignificant damage to fibre tracts overlying the BZ showed better performance postoperatively than preoperatively.

In the reaching task, three animals, one with a RTZ lesion, one with a ML lesion, and one with a RZ lesion, showed depressed performance scores. These scores, however, may be considered spurious for reasons outlined below (sec. 6.1.3). Otherwise, the only significant difference obtained was that between the RZ group and the non-lesioned animals (Sham-Op and Normal Control combined) on the Training

measure (trials to criterion).

CHAPTER 6

DISCUSSION

The primary experimental hypothesis--that lesioning the RTZ will produce motor deficits similar to those observed previously in DC-Lesioned animals--was confirmed with one animal in the acquisition condition of this study. In comparison to Sham-Operated Control animals, this animal's performance was affected in both the walking task and the reaching task. Another animal, lesioned in the cyto-architectural border zone (BZ) between the RZ and the rostral portion of the RTZ, showed an even more severe beam-walking impairment. This BZ animal, which walked preoperatively with fewer errors than any of the other Normal Control animals, made more errors postoperatively than any other animal.

The corollary hypotheses--that lesions of the RZ and ML should not produce motor deficits--were not confirmed, although the present results require additional interpretatior (see sec. 6.1). A group of animals displaying massive damage in the RZ failed to perform as well as Sham-Ops in the walking task. They were also the only animals in which a statistically significant reaching deficit could be detected, but this was only in one of the measures used. (The apparent severe reaching deficits of C-125 and C-153 require additional interpretation. see sec. 6.1.3). The ML animals also performed more poorly than the Sham-Op animals in the walking task. They were, however, significantly less impaired than the RZ animals. This relative lack of impairment occurred in spite of the fact that two of the ML animals were blind.

Two animals which presented insignificant damage to fibres

overlying the BZ actually performed better postoperatively than preoperatively in the walking task. Their postoperative and preoperative performances did not systematically differ in the reaching task.

The RZ, RTZ, and BZ animals showed improvement in walking task performance over the postoperative testing period. The less severely affected ML animals did not show significant improvement. Neither did the performance of the Normal Control and Sham-Op animals.

Finally, the Normal Control and Sham-Op animals differed significantly from one another in only one walking task measure.

Before drawing conclusions from these results, it is necessary to consider certain issues of interpretation which tend to mitigate some of the conclusions and augment others.

6.1 Issues of Interpretation

6.1.1 Recovery vs. Compensation

The deficits of all the DCN-Lesioned animals in the walking task were characterized by early severely subnormal performance followed by improvement over the testing period. The RZ-Lesioned animals, moreover, could not be differentiated from non-lesioned animals in the reaching task by post-criterion performance, yet they required significantly more training trials to achieve criterion performance.

There are three alternative explanations of these results: (1) The deficits accompanying DCN lesion are a temporary debilitation related to general surgical trauma. (2) Improvement in performance is related to physiological recovery within lesioned systems. (3) Lesion effects endure, but animals are able to behaviorally compensate for them in specific task situations.

There is little doubt that the first alternative applied in the early stages of postoperative recovery. Recall (sec. 5.2.1) that the Sham-Operated animals showed walking and reflex debilitation under casual observation until the fifth postoperative day. Recall also, however, that two of these animals did not completely recover from anesthetic for at least two days. The Superficial BZ animals, on the other hand, recovered from anesthetic fully within eighteen hours (sec. 5.2.4). Neither of these BZ animals ever showed any sign of disability. This early recovery was in spite of the fact that one of these animals bled profusely during surgery, and the fact that lesions had been attempted in these animals. Thus it is concluded that factors relating to general surgical manipulation such as anesthetic susceptability, dosage control, bleeding and edema, are sufficiently variable in their effects so as to render very early observation of deficit uninterpretable as a lesion effect. Whatever the early consequences of surgical manipulation alone, these cannot be considered to be having an effect on task performance, since their time course is much shorter than the period of time allowed to elapse between surgery and postoperative testing (at least 15 days). Similar effects in lesioned animals, however, often lasted well beyond this postoperative recovery period.

The second alternative, that gradual improvement in performance may be due to physiological recovery in lesioned systems, also cannot be supported by the present results. First of all, those animals which registered the most severe deficits in the walking task situation showed abnormalities in reflexes and/or walking under casual observation

which endured the entire period of postoperative survival (sec. 5.2), from 45 to 98 days. This was in spite of their improvement in task performance. This is consistent with alternative (3) above, that practice fosters behavioral compensation in specific task situations in spite of an enduring lesion-produced deficit.

Sjoqvist and Weinstein (1942) reported such behavioral compensation in their DC and ML lesion studies of lower primates. These monkeys and apes were able to get around in their environment, after a period of postoperative recovery, about as well as before lesioning. Yet their movements, in the words of the authors, were "slow and deliberate," lacking the "playful abandon" characteristic of these species. Something of the same sort was observed in the present walking task. C-7 (BZ), for instance, though he could by the end of the testing period traverse the beam with few errors, tended to wobble and step much more slowly than he had done preoperatively. C-49 (RZ) always moved slowly and deliberately, in a relatively crouched position. Even though preoperative observations were not available on this animal, no non-lesioned animal walked the beam in a similar manner. Their walking was marked by customary feline grace and rapidity.

It is evident from the relatively better postoperative beam-walking performance of the preoperatively trained Superficial BZ animals (sec. 5.3.2) that practice in the walking task improves performance. This result further argues that the practice effect survives a minimal-lesion surgical intervention. In fact, had the hypothesis-testing structure of these experiments allowed a one-tailed

comparison based on the prediction of better postoperative performance, (see sec. 6.2.1), the Superficial BZ animals would have scored significantly fewer Pivoting Errors and Falls than the Normal Controls.

Another piece of evidence mitigating against the physiological recovery explanation of improvement is that terminal evoked potential experiments showed no detectable recovery of lemniscal transmission in the RZ, RTZ, or BZ-Lesioned animals (sec. 5.1.1). It can, however, be argued that the evoked potential data gathered in this study is unreliable, since postoperative amplitudes do not conform systematically to the observed degree of lesioning. For instance, the Sham-Op animals show declines in evoked potential amplitude (Figs. 3a., 3b.) not shown by the mininally-lesioned Superficial BZ animals (Figs. 6a., 6b.). Also, there is some variability in postoperative evoked potentials within the RZ group (compare Figs. 4a., 4b., 4d.).

The results of this study are suggestive, rather than conclusive, of a lesion-produced deficit which is mitigated by practice. In order to demonstrate this conslusively, further experiments are needed. For instance, a group of lesioned animals would be sensorily and motorily deprived for a period of weeks and then tested. If they performed well, then physiological recovery would be presumed. If they failed to perform well, then they would continue to be tested in order to assess their post-lesion improvement curves. If such curves were equivalent to those which could be plotted from the data in the present study, then compensation would be presumed. If they were steeper, an interaction of recovery and compensation would be concluded. If they were less steep, it would be concluded that the lesion, in addition to

subsequent deprivation, had impeded an interactive process of physiological recovery and behavioral compensation.

6.1.2 Reticular Zone Deficit

Given the present results, what can be said in regard of their applicability to the hypotheses being tested, i.e., do RTZ lesions produce motor deficits? Do lesions to the RZ and the ML, presumably areas engaged in the relay of sensory information rather than the integration of kinesthetic inputs into ongoing motor activity, fail to do so?

The appearance of walking deficits following RZ and BZ lesions run counter to the prediction that only RTZ lesioning should produce motor deficits. Recall, however (sec. 5.1.1), that the RZ and BZ lesioned animals displayed total or near-total transsection of fibre tracts passing over the RZ in the dorsal superficial aspect.

Basbaum and Hand (1973) present anatomical evidence that, in the rat, some DC fibres project to the RTZ superficially over more caudal zones of DCN afferent termination. This evidence is consistent with the present histological finding that as progressively more frontal sections of the DCN are viewed, the superficial fibres are gradually replaced by cellular material until no more fibres are seen. Thus, removal of input to RTZ kinesthetic-integrative functioning is tentatively indicated in the walking deficits of the RZ and BZ animals. In other words, RZ and BZ lesions do not selectively interrupt afferent inflow to sensory processing, but involve RTZ functioning as well.

In order to verify that RZ lesions alone do not affect motor

performance, it would be necessary to discretely lesion the deep nuclear areas of the RZ, leaving the superficial fibres intact. This might be accomplished by carefully controlled electrolytic means. In order to assess the importance of the superficial fibres in motor performance, it would be necessary to lesion them independently in other animals.

This problem of anatomic overlap of RTZ and RZ components was originally anticipated and was the reason (sec. 3.3) for testing a group of ML-Lesioned animals. Presumably, such lesions would interrupt transmission only in the sensory pathway which departs the RZ, leaving motor function relatively undisturbed. In line with the present hypotheses, this experimental "backup" procedure resulted in motor deficits which were much less severe than those produced by RZ, RTZ, or BZ lesioning. This occurred in spite of the fact that two of the three ML animals were blind. Furthermore, note (Figs. 3, 4) that the walking performance of the blind ML animals (C-118, C-203 was worse than that of the sighted ML animal (C-153). Were ML lesions to be repeated in more animals without blinding them, it might be found that the present mild ML-related deficit is attributable to the blindness alone.

A further argument in favor of the relative importance of the RTZ for motor functioning is the relative strength of the deficits seen in the BZ and the RTZ animals. The BZ animal's walking deficit was the strongest one recorded (Figs. 3, 4). This is in spite of possible practice effects carrying over from preoperative training, such as were identified in the Superficial BZ animals (sec. 6.1.1). The RTZ

animal also showed a strong walking impairment, though more animals with RTZ lesions are required to establish its relative strength statistically.

6.1.3 Interpretability of Reaching Task Results

Note that discussion so far has centered primarily on the walking task results. This is because the reaching task results yielded little useful information. The only statistically significant difference obtained was that between the Sham-Op and RZ animals in the Training measure. This is perhaps due to a RZ lesion-related deficit which improves with practice. Hence no significant differences occur in any of the post-criterion measures. Such an interpretation is consistent with the initial severe RZ lesion-related walking deficit, followed by improvement over the postoperative testing period.

In addition to the statistically significant difference reported above, one is also tempted to interpret the poor post-criterion performances of the RTZ animal and the one testable ML animal (see Figs. 12-14) as being lesion-related. Aside from such single instances of performance being inconclusive, the scoring techniques used are sensitive to idiosyncratic strategies which animals develop in learning to reach for and obtain bait. In addition, they are sensitive to variations in motivation.

6.1.3.1 Strategy. On the face of things, the reaching task appears to be a more complex task than the walking task. Unlike the walking task, it requires that animals precisely adjust the projection of body and limb to the anticipated position of a moving object. The notion that the task is more difficult is reinforced by the fact

that animals must be coaxed and cajoled into making an overhead reach, and that reaching for bait on a moving disc can only be trained when the animal has first been induced to make the overhead reach. On the other hand, even animals with strong deficits will readily walk a beam with relatively little training. In the present study, animals were trained to walk the beam in no more than four training periods. The reaching task, however, was trainable in no less than eight periods.

However, this very difference, the relatively large amount of practice given in the reaching task, allows the development of individual strategies for reaching which confound attempts to separate animals by the measures of performance used.

For example, C-52 (RZ group, Figs. 11-14) developed a well-directed and usually highly precise two-pawed snatch during training. With this technique, bait, when taken from the disc, was usually carried directly to the mouth before the forepaws struck the floor again. Other animals, for the most part, reached with one paw or the other in a less well-directed fashion. They would slide the paw along the bait holder and pull or bat the bait off from behind, rather than reach for the bait itself. Note, however, that the strategy of C-52, which involved more refined reaching, was actually less effective in terms of Training, Efficiency, and Accuracy scores than the predominant "slide and pull" method. C-52's Tracking performance, on the other hand, falls somewhat in the middle range. This shows that while the reaching strategy itself may have led to a poorer performance overall, this animal was not particularly impaired in locating bait when it failed to make its "instant snatch" and the

bait fell to the floor instead.

C-125, the RTZ animal, also developed such a strategy. Its profile of reaching scores is similar to that of C-52. Thus, until further replications, the scores alone do not imply a deficit. On the positive side, however, this animal did show an inability to maintain a two-point hindlimb stance for any longer than the actual thrust of the reach. It often also fell over backwards, a behavior displayed by no other animal in this study. This animal's rather striking and unique hindlimb disability has already been noted (sec. 5.2.3) and will be taken up again below (sec. 6.4).

6.1.3.2 Motivation. The poor reaching performance of C-153 (ML group, Figs. 11-14) in all scoring categories is probably related more to the animal's motivation than any motor or sensory deficit. This animal was the only one trained in the reaching task for which the three-minute latency limit for termination of trials on a given training day (sec. 4.2.2.2) was exercised. It was, moreover, exercised on 10 of this animal's 21 days of training. If these 10 days are not considered, the number of training periods required to train this animal to criterion is actually slightly less than the mean for this study ($\bar{X}$ = 11.3 days). This is evidence that the animal possessed at least average ability to learn, but was an "underachiever."

Both during training and testing this animal was generally lethargic and unenthusiastic. This was not true for any other animal which was trainable. C-153 often sat in a corner of the experimental enclosure for a prolonged period cleaning itself. It

often gave up the task to explore its surroundings.

Motivation rather than deficit is implicated in this animal's poor Accuracy score. Its reach was well-directed but laconic, lacking sufficient force to dislodge bait even when contact with it was made. The animal also seemed uninterested in whether or not bait had actually been dislodged and fallen to the floor. After a reach, it would often turn away and pursue some other activity, whether the bait had fallen or not. This is at least partially responsible for relatively poor Tracking score of this animal. Had the relative times that animals took to consume bait after localizing it been taken into account in the Tracking score, this animal's score would have been much worse. C-153 would often approach the fallen bait, sniff it, but then back away. Sometimes it would not eat the bait for several minutes. Such was not the case with other animals, which enthusiastically consumed the bait as soon as it had been localized.

6.1.4 Conclusions

From the present work certain tentative conclusions are offered:

1. The walking deficits observed in the RTZ, BZ, RZ, and ML-Lesioned animals were produced by the lesions themselves. They were not a by-product of general surgical recovery, as Sham-Operated and minimally lesioned animals showed no signs of deficit lasting past the first week. Some of the most severely affected lesioned animals actually recovered consciousness and showed activity earlier than the Sham-Ops (sec. 5.2), yet some of their deficit signs persisted until sacrifice.

2. The improvement seen in the performance of the RZ, BZ, and

RTZ animals over the postoperative testing period is due neither to prolonged surgical recovery necessitated by an actual incursion into the brainstem not to recovery of function in lesioned pathways. Rather, it represents a behavioral compensation, by as yet unidentified mechanisms, as a result of practice in the test situation. To this point, the most severely affected animals retained walking and/or reflex abnormalities in spite of improvement on the task itself. These animals also appeared to move with great deliberateness in some cases, compared to the more carefree beam-walking of non-lesioned animals. Practice effects, transcending attempted lesion manipulation, were identified in two animals. These effects imply that walking task performance may improve with practice even in lesioned animals, again supporting the notion of behavioral compensation.

3. Motor deficits are caused by disrupting a function of the RTZ in the integration of afferent inputs into motor activity. The existence of motor deficits in RZ and BZ animals is in apparent contradiction to this. Yet these animals showed interruption of fibre tracts which apparently project through the RZ to the RTZ. Anatomical and lesion experiments are required in order to clarify this last point. ML lesions, however, which presumably interrupt the sensory relay outputs from the RZ, result in only a mild walking deficit. They also produce no lasting reflex or walking deficits detectable by casual observation. Even the mild walking deficit may have been a by-product of the fact that two of the three ML animals were blind.

4. Strategies which animals adopt during prolonged training are

capable of strongly influencing scores in the reaching task. Such influences may give a false impression of deficit where none exists or obscure group differences where a deficit does exist. Motivational factors have similar influences.

6.2 The Study as Planned vs. The Study as Executed

The statistical testing of prior hypotheses requires that experimental groups and the numbers within them required to achieve significant differences be chosen in advance. In lesion studies, however, such a preplanned approach is difficult to execute. First of all, as in the present study, survival rates for previously unattempted and technically difficult lesions may be low. Secondly, formation of experimental groups depends on lesion histology, i.e., animals may be trained, tested, and then sacrificed, only to find that the appropriate lesions have not been made in some animals.

Two courses are open to the experimenter if, as in this study, these factors result in unfilled experimental groups and the formation of unplanned groups: (1) He may continue to refine techniques and lesion animals until the originally planned groups have been filled. However, this requires a liberal endowment of both time and money. (2) On the other hand, he may alter statistical hypotheses somewhat to accommodate the data obtained. This is the alternative which has been chosen in the present report.

It is, however, debatable as to whether or not statistical testing is really necessary in cases where lesions produce spectacular and unmistakable deficits. In the present work, the RTZ and BZ lesions produced such deficits. Naturally, in cases where only

one example of unmistakeable deficit exists, as with the RTZ and BZ lesions, one hopes to be able to replicate such deficit in at least one more animal.

Thus, statistical testing becomes a sort of "backup" insurance, in case deficits are obtained which are not readily observable, when it is necessary to carefully examine the data for differences which might indicate them. As it was, this type of insurance was desired, not only as a method of detecting inobvious differences, but partially as an heuristic exercise.

The next section describes the hypothesis testing structure as intended and as restructured to fit the data obtained. The section which follows the next suggests means by which the chances of survival of RTZ-Lesioned animals might be improved, thus making possible a more conclusive test of the primary hypothesis of this thesis.

6.2.1 Statistical Considerations

The numbers of animals originally intended to fill each of the experimental groups (sec. 4.1) were chosen on the basis of certain guidelines set forth by Rule (1976). These guidelines refer to permissable p. alpha levels for various classes of comparisons within a multiple-comparison hypothesis testing situation. Thus the intended numbers in groups were chosen to fit the minimum necessary to allow significance at an alpha level of 0.05 with the Mann-Whitney U (Siegel, 1956) for the following comparisons:

1. Retention: Normal Control to Preoperatively Trained RTZ Animals
2. Acquisition:

2a. Sham-Op to Postoperatively Training RTZ Animals

2b. Sham-Op to Postoperatively Trained RZ Animals

2c. Sham-Op to Postoperatively Trained ML Animals.

The "essential" (Rule, 1976) comparisons are 1 and 2a. That is, they are the comparisons necessary for testing the primary hypotheses, that retention and acquisition in motor tasks is affected by RTZ lesions. Comparisons 2b. and 2c. are neither "essential" nor "non-essential" in the sense suggested by Rule. They belong, instead, to a third class of comparisons in which the roles of Type I and Type II errors are reversed. That is, they are tests of assumptions the experimenter is willing to accept (no deficit caused by RZ or ML lesions) unless contrary evidence is introduced. Setting an experimentwise error rate for these two comparisons separately from that for comparison 2a. is essentially what allows hypothesis testing to take place with the small numbers of animals originally planned.

Since the originally planned experimental groups were not filled, and since one unexpected group was created, it became necessary to revise the hypothesis testing structure for these experiments. The new comparisons became:

1. Retention: Normal Control to Preoperatively Trained Superficial BZ Animals

2. Acquisition:

2a. Postoperatively Trained ML to Postoperatively Trained RZ Animals

2b. Sham-Op to Postoperatively Trained RZ Animals

2c. Sham-Op to Postoperatively Trained ML Animals.

Although comparisons 1 and 2a. are altered from the preplanned case, the prediction of differences and the direction of this prediction are not. Since the obtained experimental groups correspond, at least in number, to the original ones, they are controlled at their originally planned experimentwise error rates. Again, in comparisons 2b. and 2c., the role of Type I and Type II error is reversed, and an experimentwise error rate is established for these two comparisons separately. Since the originally planned numbers are available for comparison 2a., nothing changes from the originally planned case. Thus, in the end, only comparison 2c., identical in both the preplanned and the post-hoc cases, is affected. This is because one less ML animal is available than is needed for the original comparison. Thus, for this comparison, the restrictions of p. alpha have been liberalized slightly to allow statistical significance at an error rate slightly higher than that originally intended. Note that by allowing this, damage is done to one of the hypotheses, namely, that ML lesioning should <u>not</u> result in deficits. Thus, by following current practices in regard of hypothesis testing (Rule, 1976), this slight difference would not have been interpreted as a deficit.

In order to fill out the originally planned experimental groups so as to allow statistical testing of the prior hypotheses, five more lesioned animals are required. These are two preoperatively trained RTZ animals, two postoperatively trained RTZ animals, and one postoperatively trained ML animal. More animals would be needed to fill in for those not trainable in the reaching task. However, since this task appears insensitive to deficit under the present conditions

(sec. 6.1.3), its future use in filling out the present set of data is not comtemplated.

6.2.2 Improving RTZ Lesion Techniques

Even though RTZ lesion deficits may be conspicuous enough to obviate the need for their statistical demonstration, the one successful RTZ-Lesioned animal in the present work is not sufficient to conclusively demonstrate those deficits. Thus at least one replication is desirable before the results of the present work are published. Preferably, the full compliment of the originally planned groups should be obtained.

Certain technical problems regarding control of the depth and sanguinity of RTZ lesions still remain (sec. 5.1.2). These must be solved in order to ensure the survival of RTZ animals in the future. To this end the following precautions are suggested:

1. In order to prevent accumulation of blood and thus fatal buildup of pressure in the fourth ventricle, a cannula should be inserted between the cerebellum and the brainstem to allow drainage to the exterior. Several varieties of small, highly pliable cannulae are available which might be used.

2. The heat-lesioning probe should not be manipulated by hand. Rather, it should be moved into the lesion site by means of a stereotaxic manipulator.

3. A soldering iron with a rapid rising time and a low heat capacitance should be used. This would allow manipulation of a cold iron into and out of the lesion site. Several makes of small, battery-powered soldering irons are available which might be adapted.

Changing to a relatively low heat capacitance would require preliminary calibration of lesion sizes to various time-temperature combinations. This would have to be undertaken on living preparations before RTZ lesioning parameters could be established.

6.3 Comparison of the Present and Previous Work

6.3.1 Walking Task

Melzack and Bridges (1971) obtained results similar to those of the present work in that lesions of the more caudal portions of the DCN (presumed to be equivalent to the RZ in this work), including fibres projecting more rostrally, produced significant beam-walking deficits in cats. One of the DCN animals in that study showed, in addition, complete lesioning of the decussation of the ML. This animal's deficit, however, was not especially strong. This is consistent with the present notion that this presumably sensory pathway does not make an important contribution to motor control.

In the Melzack and Bridges study, animals wtth cervical DC lesions showed more severe walking deficits than animals with DCN lesions. The relative severity of the DC deficits may have been due to apparent dorsolateral tract involvement in some of the lesions. Recall (sec. 2.1, 2.3.1, 3.2.2) that many kinesthetic fibres which enter the DC from the hindlimbs leave the columns at the thoraco-lumbar border, thereafter ascending in the dorsolateral tracts. Thus, the combined interruption of DC and dorsolateral pathways would be expected to produce a more severe motor deficit than DC lesion alone. Such is often the case with sensory deficits (sec. 2.3.1).

Another possible explanation of the relatively mild DCN deficits in the previous study is that parts of the DCN were left intact in the ventral aspect. Recall (sec. 3.2.1) that the RTZ wraps itself around the RZ ventrally. Thus, whereas the fibres passing over the RZ were severed, probably affecting RTZ function (sec. 6.1.2), most of the ventral and rostral components of the RTZ, along with their non-DC inputs (sec. 3.2.2), remained intact, tending to mitigate lesion effects.

In order to compare the effects of DC lesion to the effects of the DCN lesions in the present study, it would be necessary to test DC-Lesioned animals under the present conditions. These conditions differ slightly from those of the previous study in terms of scoring methods and length of postoperative testing.

6.3.2 Reaching Task

Dubrovsky and Garcia-Rill (1973) and Dubrovsky et al. (1971), obtained strong deficits in a reaching task similar to the present one with DC lesions in cats. Their results are more impressive than the present work results for two reasons: (1) Two months was allowed to elapse between surgery and the beginning of training, compared to the 15-28 days allowed in the present study. This permitted, under their conditions, much time for general behavioral compensation and/or physiological recovery. Beck (1973) reports that such a period of postoperative recovery/compensation is sufficient for DC-Lesioned squirrel monkeys to achieve performance levels matching those of non-lesioned animals on a task requiring agility and object-movement anticipation. (2) The DC reaching

deficits obtained by the Dubrovsky group perservere even in the face of extensive training. In one series of animals, preoperative training did not mitigate the postoperative deficit. In another series, in which 600 trials were added both preoperatively and postoperatively to the usual 300 trials used in testing, a deficit was still obtained. In this case, the deficit was slightly less severe, yet it is nonetheless clear that it was resistant to behavioral compensation, unlike the mild, transient deficit detected in the present RZ animals.

Again, in order to assess whether the differences between the studies are due to relative mildness of DCN lesions compared to DC lesions, it is necessary to test DC animals under the conditions of the present study. On the other hand, it is possible that, under more rigorous task conditions, the DCN lesions of the present study would yield deficits as definite as those obtained by the Dubrovsky group. In fact, the previous deficits were obtained under task conditions more difficult than those of the present study.

For instance, the lower edge of the disc used in the present work rested 4.6 cm. closer to the floor than that used by the Dubrovsky group. It seems unlikely, however, that this could have been the major cause of the differences between the studies. This lower height still required that most of the animals in the present study leap, as did the height used in the previous studies. Yet in one series of experiments, the previous workers lowered the disc such that all animals could reach bait by rearing and reaching, rather than leaping. In that series, a deficit was still obtained.

The Dubrovsky group also utilized a faster disc speed and a

larger disc than in the present study. Thus the velocity of the bait at the edge was 22.4 per cent greater in the previous work (0.97m./sec.: 1.25 m./sec.). Thus, a certain "bait-velocity" may be sufficient to separate debilitated animals from controls, while a slightly lower velocity may not. In addition, the maximum bait velocity of the present study was used in only the last five of the ten testing days (sec. 4.2.2.3). The previous authors apparently used their bait velocity over the entire post-criterion testing period.

Training differences between the studies are difficult to assess, since little information regarding training is provided by the previous authors. Yet it is possible that their animals began testing at a lower level of performance. If training differences alone are involved, however, one would expect that in their 900-trials preoperative/900-trials postoperative series, performance would improve at least to the levels of the present study if the animals had begun testing originally at a lower level of performance. The maximum number of trials any animal required to complete testing in the present study was 497. Only one other animal required more than 300 trials.

If further attempts are undertaken to identify a DCN reaching deficit, then testing conditions must be made, as nearly as possible, identical to those in which DC related deficits are reliably obtained. Thus: (1) The authors of earlier papers should be directly consulted for details of their training procedures. (2) A task of precisely equivalent difficulty to that of the previous studies should be used. Thus the mild deficit of the present study, which

showed up only as an early tendency, might be uncovered more fully. (3) Cumulative daily records of differences between groups should be kept on an ongoing basis. These would be explored for tendencies such as an early increasing performance difference between experimental and control groups, mitigated later by practice. Statistical comparisons designed to uncover lesion effects would then be made for that point in training/testing at which accumulated differences would be maximal.

6.3.3 Summary and Implications

Melzack and Bridges (1971) obtained beam walking deficits with DCN lesions. These lesions were similar to the RZ lesions of the present study. These DCN lesion deficits were less severe than DC deficits obtained in the same study. Because of certain procedural differences between the present work and the previous work, it is not possible at this time to assert whether the present DCN deficits are equivalent to those of the previous work.

The Dubrovsky group (Dubrovsky & Garcia-Rill, 1973; Dubrovsky, et al., 1971) obtained severe reaching deficits compared to the mild and transient reaching deficits obtained in the present work. These differences may be due to the difference in lesions or to the slightly more difficult task used by the previous authors. They may be due to both. In order to assess the importance of the task variables, testing of DC-Lesioned animals under the conditions of the present study is necessary. In order to make DCN-Lesion results comparable to previous DC-Lesion results, it is necessary to test DCN-Lesioned animals under the previous conditions.

If task differences between this and the previous studies are ignored, comparison of their results suggests that RZ lesions produce a strong walking deficit and a weak reaching deficit. Recall, however, that nothing in the original experimental hypotheses (sec. 3.3) suggests that the two tasks measure different things. They are both intended simply to provide a general index of motor ability.

Recall also (sec. 2.4.2) that DC lesions do not produce as severe deficits in brief motor sequences (such as anticipatory reaching and jumping) as they do in longer ones (such as walking two lengths of beam). This corresponds to the RZ-Lesion results in the present study. Yet it can be argued that in a longer behavior sequence there is more probability of error and hence more likelihood of identifying a lesion-related deficit, given a relatively errorless non-lesion baseline. Thus the apparent task difference in the present study may simply be a measurement artifact. To reiterate, no fundamental conclusions can be drawn regarding the specificity of RZ lesions for certain types of deficits.

6.4 The Nature of DCN Motor Deficits

What has been observed in the present work is, at most, the correlation of deficit with lesion. Inferences can be made from such observations regarding the anatomical locations in which certain forms of processing may occur. Thus, by the evidence presented in this study, it has been concluded (sec. 6.1.4) that RTZ lesions abrogate the integration of kinesthetic afferent inputs into the control of motor activity. This conclusion is tentative, pending further replications of RTZ lesions.

Incidental observations may provide certain clues regarding the specific nature of the deficits produced. A case in point is the peculiar and unique hindlimb deficit observed in the RTZ animal (sec. 5.2.3).

Recall (sec. 2.3.1) that other researchers have found motor deficits in the forelimbs of various species to be more pronounced than those in the hindlimbs following cervical DC section. Thus the result with the RTZ animal is an anomaly. It is not likely to be a species-specific effect of general DC system damage in cats, since it appeared in no other animal in this study.

It is surmised (Mountcastle, 1974) that the joint movement and deep tissue afferent components which project preferentially to the RTZ (sec. 3.2; 3.3) do so by means of the dorsolateral columns. Recall (sec. 2.3.1) that many kinesthetic fibres depart the DC at the thoraco-lumbar border and that many of these ascend via the dorsolateral columns (sec. 2.1; 2.3.1; 3.2.2). It is possible that many are fibres from the hindlimb which provide inputs into the RTZ necessary for limb coordination. Thus, while cervical DC lesioning would be expected to preferentially disrupt kinesthetic input from the forelimbs into the RTZ because of the exclusivity of such transmission (sec. 2.3.1; 3.2.2), RTZ lesioning would be expected to preferentially exert an effect on the hindlimbs.

This speculation is, of course, tempered by the fact that an outstanding hindlimb deficit was obtained in only one animal. Were further RTZ-Lesioned animals to show similar behavior, it might then be useful to electrophysiologically study the relative forelimb

and hindlimb contributions of the kinesthetic modalities to the rostral portion of the RTZ.

One might speculate also that the RZ exerts a "preparatory alerting" influence on RTZ kinesthetic-motor integration. Rapidly conducting impulses arriving by the monosynaptic reflex route selectively prime RTZ units which receive slower kinesthetic inputs from the same dermatomes as the rapid inputs. This priming may be sufficient to initiate, in turn, a similar priming of units in motor nuclei. When the slower kinesthetic impulse has arrived, even if it related to a wider dermatomal area than the previous fast impulse, only the pathway to movement selectively primed will be excited fully, and only the appropriate movements will occur. Such a notion is consistent with the primarily facilatory nature of various influences on RTZ units (sec. 3.2.4; 3.2.5) and the intimate connection of the RTZ with brainstem nuclei involved in the initiation and control of movement (sec. 3.2.6). Such selective priming of pathways for motion upon the receipt of kinesthetic impulses may also occur via descending cortical routes. Descending cortical influences on the DCN are primarily facilatory (sec. 3.2.4).

Such ideas are not inconsistent with models of DC-system function in movement which invoke a "filter setting" function of rapidly arriving inputs and/or cortex (Wall, 1970). Except in the present speculation, the emphasis is laid upon facilitation, rather than dampening, of input routes.

Ascending preparatory facilitation may also open up routes to specific movements in the presence of some more general command for

activity, i.e., it may be a way general commands for movement become adapted to the precise exingencies of an ongoing sequence of movements in given environmental conditions. DC lesion would interrupt the fast "alerting" component of such a system. RTZ lesion would disrupt the system at its first facilatory switching station. Either way, the outcome would be the same: movements which show directedness but which are not well-adapted to specific stimulus situations.

Something of the same sort has been argued by Melzack (Melzack & Bridges, 1971; Melzack & Southmayd, 1974). According to speculation in those papers, the DC system serves an important role in providing rapid input into central processing systems which must select one of a number of possible alternative movement sequences in response to situational factors and active proximal and distal goals of movement. The idea is the same as the present one, in that DC inputs provide information by which adaptation to the situation is formed. The idea is different in that it requires activation of specific stereotyped "motor programs" which must then be sequenced together by the central processor. It is certain that such programs exist, since stimulation of certain areas of the brainstem and midbrain are capable of eliciting stereotyped sequences, which are nonetheless adapted to the situation (Hess, 1957; Pinneo, 1956). The stereotyped yet coordinated nature of "fixed action patterns" which are released by specific sign stimuli is well known (Lorenz, 1966). Yet it is not just such stereotyped patterns which are disrupted by DC or DCN lesion, but all activity in which the animal engages.

The present ideas allow more flexibility, in that general

directives for movement interact at brainstem levels with afferent inputs to produce adaptive movement. They are also simpler, in that a complex sequence of input - cognition - program selection - activation need not be invoked, as they have been in previous speculations. Furthermore, there is probably little cerebellar contribution to this processing since animals in the present study were able to reach, and did so without characteristic cerebellar tremor (Dow & Moruzzi, 1958).

Another speculation which receives support from previous work is that the RTZ serves to dampen down activity in the rapid sensory pathways relaying from the RZ during periods of active movement. Dampening of DCN evoked potentials (presumably only sensory-lemniscal in nature) has already been observed during and shortly before active movements (sec. 2.4). It is reasonable to presume that this is mediated in the RTZ because of the preferential projection of descending cortical influences to this area and the fact that only inhibitory cortical effects have been observed in the RZ (sec. 3.2.4).

Thus, by the present speculations, a complex dual interaction may exist between the RZ and RTZ. In this dual interaction, the rapid inputs to the RZ facilitate, through the RTZ, pathways to movement specifically adapted to the stimulus situation. Secondly, once a movement has been initiated, such "priming" of motor pathways is dampened down by massive RTZ activation, either by way of descending cortical influences or kinesthetic input. If such is the case, critical experiments at the cellular level during active movement still remain to be done.

One problem in identifying the specific nature of DC, DCN, or RTZ lesion deficits in experiments such as the present one and those of the Melzack and Dubrovsky groups is the arbitrary and subjective nature of the measurements used. As in the present work, a measure may have formal reliability, but lack the power to tease out specific components of deficit.

Another approach to the study of DC related motor deficits which has not yet been considered would take as its starting point the now extensive body of knowledge which has accumulated on the kinesiology of cat walking (Wetzel, 1976). The arbitrary selection of scoring categories and of units of sequential movement which characterizes this and previous studies need not continue to be the case. It is now (and has been for a long time) possible to describe deficits produced by lesions in terms of well-defined parameters of stepping. Looking at stepping deficits in such a framework would give a clearer notion of where to begin looking for neural explanations of those deficits. Unfortunately, the tapes made of walking sequences in the present study are useless for such work, since they picture animals end-on rather than at the flanks, the orientation of the observer in most kinesiological work.

6.5 The DC System in Sensation--Suggestions for Further Work

Returning to the unsolved problem of the sensory role of the DC system, some suggestions are now made regarding approaches which researchers might use in the future in attempting to define it. One approach, the study of DC mediated sensation in the isolated DC preparation, has already been discussed (sec. 2.3.4).

The few findings of the four studies in which such preparations were used are as yet tentative, and on some points apparently contradictory. Even were further experiments with such preparations to demonstrate conclusively that fine, motion-related discrimination survives and can be formed following anteriolateral cordotomy, it would still not be proved that the DC system subserves such functioning in the intact animal, or that it is the only system capable of doing so. In fact, as emphasized by the study of Vierck (1974; sec. 2.3.4;3.1) the DC sensory function probably overlaps with sensory function in other ascending pathways, even though it may also maintain some exclusive features.

In order to demonstrate or disconfirm an allegation that the DC subserves a given discrimination in the intact animal, and that it is the only system capable of doing so, the second part of any programmatic approach would be to couple DC lesion experiments with previous isolated-DC experiments in which continuation of sensory function had been observed. Comparisons of maintenance, loss, or potentiation of sensory resolution among whole-spinal, isolated-DC, and DC-Lesioned preparations is vital in order to assess the relative contribution of the DC system to the whole somatic sensorium.

Split-brain preparations would make such comparisons possible in single animals, as certain experiments indicate that callosal lesions dampen interhemispheric transfer of somatosensory cues in monkeys (Semmes, et al., 1968). Thus optimal control for within-subject variance would be achieved. For example, one would simply

train the split-brain animal in a certain task, unilaterally sever both the DC and anteriolateral pathways, and study postsurgical performance. Thus changes in pretrained discrimination brought about by severing the different pathways might be compared in the same animal. With variations, the same basic paradigm could be used to study retention vs. acquisition in the same animal following one type of lesion administered bilaterally, untrained vs. retrained recovery of deficit, recovery vs. compensation in another animal, etc.

Such an approach, as innovative as it might be, will yield little information about the basic relative capacities of the DC system for temporal and spatial resolution of sensation so long as idiosyncratic discrimination tasks are used, such as evaluating differences in palpated edges, air puffs of varying intensities, or the direction of moving brushes. There is no doubt that ingenious use of such tasks (sec. 3.1) can give unforseen insights into the nature of sensory functioning. But they do little to define the system properties of a continuum of sensation and the changes they may undergo when afferent transmission is attenuated, and the different alterations of such properties which might be brought about by abrogations of different sets of inputs.

The now-classic studies of the Mountcastle group (Mountcastle, 1974; Talbot, et al., 1968) in flutter-vibration sensibility are exemplary of the kind of evaluation of sensory capacities which might be applied in isolation-lesion studies. Just as critical flicker fusion is a derived sensation which can be utilized to evaluate the temporal-resolution capacities of the human retina

(Cornsweet, 1970), flutter-vibration threshold is a derived (Mountcastle, 1974) form of sensation which can be used to study the temporal resolving capacities of somesthetic systems.

The sort of question to be asked would be: Having obtained a frequency-amplitude tuning curve for vibration threshold as in Talbot, et al. (1968), what changes in this curve would be brought about by various spinal lesions?

CHAPTER 7

SUMMARY

Beck (1975, 1976a) has reviewed evidence that the DC system may be subdivided at the level of the DCN into two anatomical and functional subcomponents. One of these, the classical lemniscal-line system of the more caudal and superficial DCN, the "Relay Zone", is assigned the high-velocity, rapidly-adapting transmission of peripheral somesthetic impingements to consciousness. The other subcomponent lying more rostral and ventral to the first, the "Reticular Zone", is implicated in integration of kinesthetic inputs into body movements on the basis of its representation of kinesthetic modalities and the often-seen motor debilitation accompanying DC lesion.

In the absence of definitive data regarding sensory function in the DC, after more than a century and a half of attempts to study it by lesion techniques, the present study was undertaken in order to determine whether motor deficits of the type obtained with DC lesion would be produced by lesions to the reticular zone. It was additionally predicted that lesions to the relay zone would not result in similar motor deficits.

Two motor tasks were used, similar to tasks used by previous authors in DC-Lesion studies. One of these required that cats walk a narrow plank in order to obtain food rewards. The other required that they snare bait from the edge of a wheel rotating rapidly in a vertical orientation over their heads.

Lesioning of the reticular zone in one cat and of a zone bordering the relay zone and reticular zone in another cat produced

a marked deficit in walking performance. A recognizable deficit in reaching performance was registered by one cat with reticular zone. Lesioning of elements of both the relay zone and reticular zone yielded a strong walking deficit in four cats and a mild reaching deficit in three cats. Three cats with lesions of the medial lemniscus, the output pathway of the relay zone, showed a mild walking deficit which was significantly less severe than that of the previously mentioned four cats. This was in spite of the fact that two of the three relay zone-only cats were functionally blind.

Though these findings need to be replicated in additional animals in order to make them statistically testable, they are consistent with theoretical predictions. That the obtained deficits are real lesion effects is upheld by the appearance of an initial severe deficit which declines with practice, while certain reflex abnormalities remain in spite of task performance improvement. This indicates that performance improvement is a product of behavioral compensation of a lesion deficit rather than general recovery from operative procedures. It is not, furthermore, due to recovery of the relay zone since terminal experiments showed no increase over post-lesion levels of lemniscal transmission.

The present findings neither support nor deny theories of DC system function which invoke complex central interactions. A simpler model of bulbar-level integration has been proposed, in which particular pathways for movement are facilitated by sensory inputs in the presence of more general descending commands.

Suggestions have been presented for strategies which may be used in better defining properties of DC system sensory function.

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